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TUBERCULOSIS OF LUNGS IN PATIENTS WITH SARCOIDOSIS, GRANULOMA ANNULARE AND LUPUS ERYTHEMATOSUS

A COMPARISON, BASED ON ROENTGENOLOGIC STATISTICS, WITH ITS INCIDENCE IN PATIENTS WITH PROVED TUBERCULOSIS OF THE SKIN AND WITH DIFFERENT STAGES OF SYPHILIS

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The etiology of sarcoidosis (lymphogranulomatosis benigna, Besnier-Boeck-Schaumann disease, sarcoid of Boeck, lupus pernio), granuloma annulare and lupus erythematosus is still undetermined. The discussion usually centers around the following possibilities: (1) a specific disease, caused by (*a*) Mycobacterium tuberculosis, (*b*) another specific micro-organism or (*c*) an unknown organism or virus, and (2) a syndrome or cutaneous reaction caused by any of a multiplicity of agents.

The association of these diseases with general tuberculosis has been used in defending as well as in refuting the possibility of a tuberculous origin. Therefore, it seems justified to report a statistical study of the incidence of tuberculosis of the lungs with these conditions.

METHOD

The statistics presented are based on the records of the radiologic department of the university dermatologic clinic at Breslau, Germany (directors, Prof. J. Jadassohn and Prof. M. Jessner), from 1925 to 1934.

The statistics concerning sarcoidosis, granuloma annulare and lupus erythematosus (table 1) are compared with analogous statistics of patients with true tuberculosis of the skin (table 2), as well as with those of syphilitic patients without tuberculous manifestations of the skin (table 3).

This seemed to afford an adequate basis for comparison. The patients came from the same environment; they were comparable as far as age and sex are concerned, and there was no selection in any group.

One disadvantage of the use of syphilitic patients as controls must be mentioned. They were examined primarily on account of the heart and aorta; it does not seem probable that active tuberculosis could escape detection, but minor residua of an old tuberculosis may have been overlooked or disregarded in some instances. If

TABLE 1.—*Incidence of Tuberculosis of the Lung in Patients with Sarcoidosis, Granuloma Annulare and Lupus Erythematosus*

Diagnosis	Sex	Number of Patients	Average Age, Years	Incidence (in Percentage) in Various Groups						
				0 Negative Findings	1 Signs of Healed Tuberculosis	2 Active Tuberculosis	2a Less Extensive Fibroid Processes	2b Extensive, Acute or Progressive Processes	3 Mottling of the Lung	Total of 1, 2 and 3
Sarcoidosis (lymphogranulomatosis benigna, sarcoid of Boeck and lupus pernio)	Total	28	41	35.8	17.9	32.1	17.9	14.2	14.2	64.2
	Male	12	42	58.4	8.3	25.0	8.3	16.7	8.3	41.6
	Female	16	41	18.8	25.0	37.5	25.0	12.5	18.7	81.2
Granuloma annulare	Total	23	25	43.5	30.5	13.0	13.0	....	13.0	56.5
	Male	6	25	33.3	50.0	....	....	....	16.7	66.7
	Female	17	25	47.0	23.5	17.7	17.7	....	11.8	53.0
Lupus erythematosus	Total	211	36	46.0	46.8	7.2	6.2	1.0	....	54.0
	Male	66	35	45.5	46.9	7.6	7.6	...	....	54.5
	Female	145	36	46.2	46.8	7.0	5.6	1.4	....	53.8

TABLE 2.—*Incidence of Tuberculosis of the Lung in Patients with True Tuberculodermas*

Diagnosis	Sex	Number of Patients	Average Age, Years	Incidence (in Percentage) in Various Groups					
				0 Negative Findings	1 Signs of Healed Tuberculosis	2 Active Tuberculosis	2a Less Extensive Fibroid Processes	2b Extensive, Acute or Progressive Processes	Total of 1 and 2
Tuberculosis cutis luposa (lupus vulgaris)	Total.....	753	31	30.3	53.7	16.0	12.4	3.6	69.7
	Male.....	294	28	30.6	52.0	17.4	13.3	4.1	69.4
	Female.....	459	33	30.0	54.7	15.3	12.0	3.3	70.0
Tuberculosis verrucosa cutis	Total.....	66	36	36.4	37.9	25.7	15.1	10.6	63.6
	Male.....	56	35	39.2	35.8	25.0	14.3	10.7	60.8
	Female.....	10	46	20.0	50.0	30.0	20.0	10.0	80.0
Tuberculosis cutis colliquativa (scrofuloderma)	Total.....	40	22	25.0	55.0	20.0	12.5	7.5	75.0
	Male.....	21	19	23.8	57.2	19.0	19.0	...	76.2
	Female.....	19	26	26.3	52.6	21.1	5.2	15.9	73.7
Tuberculosis cutis lichenoides (lichen scrofulosorum)	Total.....	8	8	25.0	50.0	25.0	25.0	...	75.0
	Male.....	3	11	....	66.7	33.3	33.3	...	100.0
	Female.....	5	7	40.0	40.0	20.0	20.0	...	60.0
Tuberculosis cutis papulonecrotica	Total (male)	4	21	50.0	50.0	....	....	...	50.0
Tuberculosis cutis follicularis disseminata (lupus miliaris faciei and rosacea-like tuberculid)	Total.....	71	37	47.9	42.3	9.8	7.0	2.8	52.1
	Male.....	15	43	46.6	53.4	...	...	...	53.4
	Female.....	56	36	48.2	39.2	12.6	9.0	3.6	51.8
Tuberculosis cutis indurativa (erythema induratum)	Total (female)	86	26	42.0	46.5	11.5	8.1	3.4	58.0
Total of tuberculodermas	Total.....	1,028	31	32.7	51.2	16.1	12.0	4.1	67.3
	Male.....	393	29	32.1	50.1	17.8	13.2	4.6	67.9
	Female.....	635	32	33.1	51.9	15.0	11.2	3.8	66.9

a roentgenogram had been taken of all the syphilitic patients, the incidence of those with signs of an old tuberculosis (group 1) probably would be larger.

The examinations were carried out by three examiners according to the same standards. Fluoroscopic examination was made in practically all cases; roentgenography was used as an additional method when the fluoroscopic technic indicated pathologic changes. During the last four years additional pictures were taken routinely of all patients with proved or suspected tuberculosis of the skin.

TABLE 3.—*Incidence of Tuberculosis of the Lung in Patients with Different Stages of Syphilis*

Diagnosis	Sex	Number of Patients	Average Age, Years	Incidence (in Percentage) in Various Groups					
				0	1	2	2a	2b	
				Negative Findings	Signs of Healed Tuberculosis	Active Tuberculosis	Less Extensive Fibroid Processes	Extensive, Acute or Progressive Processes	Total of 1 and 2
Early syphilis (primary and secondary syphilis)	Total	280	26	69.6	27.5	2.9	2.5	0.4	30.4
	Male	132	26	65.9	30.3	3.8	3.1	...	34.1
	Female	148	26	73.0	25.0	2.0	2.0	...	27.0
Tertiary syphilis	Total	352	42	61.7	34.1	4.2	3.1	1.1	38.3
	Male	148	44	61.5	33.1	5.0	3.4	2.0	38.5
	Female	204	41	61.8	34.8	3.4	2.9	0.5	38.2
Neurosyphilis	Total	60	44	60.0	33.3	6.7	6.7	...	40.0
	Male	38	45	57.9	34.2	7.9	7.9	...	42.1
	Female	22	43	63.6	31.8	4.6	4.6	...	36.4
Latent syphilis (including asymptomatic neurosyphilis)	Total	1,565	37	62.3	34.0	3.7	3.0	0.7	37.9
	Male	831	40	61.9	34.5	3.6	2.8	0.8	38.1
	Female	734	34	62.7	33.4	3.9	3.3	0.6	37.3
Prenatal syphilis	Total	227	13	71.0	26.4	2.6	2.2	0.4	29.0
	Male	93	11	70.0	30.0	...	...	...	30.0
	Female	134	14	71.6	23.9	4.5	3.7	0.8	28.4
Total of syphilis	Total	2,484	34.5	63.7	32.6	3.7	3.1	0.6	36.3
	Male	1,242	37	62.7	33.6	3.7	3.0	0.7	37.3
	Female	1,242	32	64.7	31.6	3.7	3.2	0.5	35.3

The lungs of the patients were classified as follows:

Group 0: Negative findings.

Group 1: Inactive tuberculosis, as indicated or suggested by signs such as shrinking and minor fibrous shadows of the apex, calcified lymph nodes and shadows, calcified primary complex, limited motion and adhesions of the diaphragm and obliteration of the costophrenic angle.

Group 2: Active tuberculosis. (*a*) less extensive tuberculosis of the lungs, with a tendency toward fibrosis, nodular infiltrations, and enlarged mediastinal lymph nodes, or (*b*) extensive, acute or progressing tuberculosis, such as massive chronic fibroid tuberculosis with or without cavities, early infiltrates with cavities or miliary tuberculosis.

Group 3: Mottling of the lungs (*Marmorierung*). This classification is arbitrary; it was adopted for the purpose of comparison with previous statistics. A more detailed classification may seem desirable. Roentgenologic studies performed for this special purpose[1] may use finer criteria, such as exact measurement

1. Nolte, F. A.: Röntgenologische Lungenbefunde bei extrapulmonaler Tuberkulose, Ztschr. f. Tuberk. **68**:305-323, 1933.

of the hilus and increase in this way the number of positive findings; however, my statistics are based on routine examinations.

It seems to me that the adequacy of the method employed is shown by the rather striking conformity of the results in both sexes in the larger groups.

COMMENT

It is the purpose of this paper to present further statistical data bearing on the relation of sarcoidosis, granuloma annulare and lupus erythematosus to pulmonary tuberculosis but not to enter deeply into the discussion of their causation.

Sarcoidosis.—The cause of sarcoidosis has been extensively discussed and reviewed [2] in recent years. As far as I can see, the majority of dermatologists still favor the tuberculous theory; [3] many authors, however, consider sarcoidosis a syndrome [4] in which tuberculosis,

2. (*a*) Séance spéciale du 13 mai 1934, consacrée à l'étude des sarcoïdes: IV. Etiologie, pathogénie, Bull. Soc. franç. de dermat. et syph. **41**:1296-1354, 1934. (*b*) Pautrier, L. M.: Les tuberculides, in Darier, J., and others: Nouvelle pratique dermatologique, Paris, Masson & Cie, 1936, vol. 3, pp. 675-732. (*c*) Volk, R.: Tuberkulose der Haut, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 10, pt. 1, pp. 386-404. (*d*) Fellner, M.: Die Hauttuberkulose, Dermatologica **80**:108-123, 1939.

3. (*a*) Andrews, G. C.: Sarcoidosis, in Diseases of the Skin, ed. 2, Philadelphia, W. B. Saunders Company, 1938. (*b*) Belote, G. H.: Lupus Erythematosus Disseminatus: Its Present Status, Arch. Dermat. & Syph. **39**:793-806 (May) 1939. (*c*) Goeckermann, W. H.: Sarcoids and Related Lesions: Report of Seventeen Cases; Review of the Recent Literature, ibid. **18**:237-262 (Aug.) 1928. (*d*) Jadassohn, J.: Dermatologie, Vienna, Weidmann & Co., 1938. (*e*) Montgomery, H.: Histopathology of Various Types of Cutaneous Tuberculosis, Arch. Dermat. & Syph. **35**:698-715 (April) 1937. (*f*) Nomland, R.: Hematogenous Cutaneous Tuberculosis (Sarcoid) in Negroes: Report of Six Cases, ibid. **30**: 59-75 (July) 1934. (*g*) Sulzberger, M. B.: Sarcoid of Boeck (Benign Miliary Lupoid) and Tuberculin Anergy, Am. Rev. Tuberc. **28**:734-745, 1933. (*h*) Wise, F., and Sulzberger, M. B.: Editorial Comment, in Yearbook of Dermatology and Syphilology, Chicago, Year Book Publishers, Inc., 1937, p. 151. (*i*) Ramel, E., abstracted, Wise, F., and Sulzberger, M. B.: Yearbook of Dermatology and Syphilology, Chicago, Year Book Publishers, Inc., 1936, p. 362. (*j*) Schaumann, J., and Boström, G.: On the Cellular Sensitivity to Tuberculin in Lymphogranulomatosis Benigna Schaumann as Exhibited in Examinations of Isolated Slices of Skin, Acta dermat.-venereol. **18**:90-101, 1937. (*k*) Grillo, V.: Contributo alla malattia di Besnier-Boeck, una fase sarcoidea della infezione tubercolare, Gior. ital. di dermat. e sif. **79**:647-669, 1938; Riproduzione delle lesioni istologiche della malattia di Besnier-Boeck-Schaumann in gangli linfactici di cavie inoculate in peritoneo con spappolato di tessuto (sarcoideo), Arch. ital. di med. sper. **4**:515-522, 1939. (*l*) Cortella, E.: Sopra un caso di malattia di Schaumann-Besnier-Boeck e di sarcoide Darier-Roussy, Riforma med. **54**:1339-1346, 1938.

4. Michelson, H. E., and Becker, F. T.: Uveoparotitis: A Sarcoid Reaction, Arch. Dermat. & Syph. **39**:329-344 (Feb.) 1939. Danbolt, N., and Brandt, A.: Sarcoidähnliche Hauttuberkulose, durch Hühnertuberkelbazillen hervorgerufen, Arch. f. Dermat. u. Syph. **178**:76-86, 1938.

syphilis and other diseases, such as leprosy [5] and leishmaniasis,[6] play roles or classify it as a separate disease of unknown origin.[7]

My statistics (table 1) show a relatively high incidence of active pulmonary tuberculosis. Of 28 patients, 4 suffered from progressive tuberculosis and 5 from a less extensive fibroid form; more or less evidence of mottling of the lungs was found in 4 more. The total number of observations, however, is small.

More impressive are those cases in which active tuberculosis of the lungs developed during observation, with or without change of the clinical picture.[8] Two of my patients belong to this group. A woman suffering from lupus pernio was free from pulmonary involvement except for shadows in one apex in 1919. In 1927 the roentgenogram showed definite mottling. A fulminating type of tuberculosis developed in 1928, from which she died. The other patient, a man, suffered for years from circinate sarcoid-like lesions of the cheek, without signs of an active tuberculosis of the lungs. Years later active tuberculosis developed, from which he died. Before his death the sarcoid lesions changed to lesions of lupus vulgaris.

It may be of interest to report the sensitivity to tuberculin (positive anergy of Jadassohn) and the incidence of osteitis tuberculosa multiplex cystoides (Jüngling), as given in tables 4 and 5. Two results may be stressed, with the necessary caution on account of the small number of cases: (1) One half of the patients, a rather high figure when compared with other statistics,[9] reacted to old tuberculin in a dilution of 1:5,000, and (2) nearly all (6 of 7) patients with osteitis multiplex cystoides gave negative reactions. The tuberculous theory, at least for the group reported on, is supported by the statistics presented.

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5. Jordon, J. W., and Osborne, E. D.: Besnier-Boeck's Disease: Report of Two Cases of Extensive Involvement, Arch. Dermat. & Syph. **35**:663-684 (April) 1937. Pillsbury, D. M.: Pulmonary Tuberculosis: Sarcoid, ibid. **33**:763-764 (April) 1936.

6. With, T. K.: Benign Lymphogranulomatosis with Special Consideration of Its Relation to Tuberculosis and Uveoparotid Fever, Nord. med. tidskr. **12**: 1787-1795, 1936; abstracted, Zentralbl. f. Haut- u. Geschlechtskr. **57**:524, 1938.

7. Kissmeyer, A., and Nielsen, J.: Notes sur l'étiologie des sarcoïdes de Boeck, Acta dermat.-venereol. **14**:283-286, 1933. Pautrier, L. M.: Les lésions oculaires de la maladie de Besnier-Boeck-Schaumann (Le syndrome de Heerfordt), Arch. d'opht. **2**:689-696, 1938.

8. (*a*) Bonnevie, P., and With, T. K.: Ein Fall von Sarcoid Boeck (Lymphogranulomatosis benigna) zur Heilung gekommen unter Entwicklung einer aktiven multiplen Tuberkulose und unter Änderung der Tuberkulinreaktivität, Arch. f. Dermat. u. Syph. **175**:407-411, 1937. (*b*) Goldschmidt, W. N.: Ueber circinär-verrucöse Umwandlung bei einem Sarkoid Boeck und eine ähnliche Form bei Lupus vulgaris, ibid. **149**:331-338, 1925. (*c*) Funk, C. F.: Boecksches Sarkoid, Lupus pernio und Lungenbeteiligung, ibid. **167**:560-577, 1933. (*d*) Nolte.[1] Volk.[2c]

9. Schaumann and Boström.[3] Funk.[8c]

Granuloma Annulare.—As far as the cause of granuloma annulare is concerned, no definite trend in the general opinion is noticeable.[10] The combination with other manifestations of tuberculosis of the skin,[11] the relation to the sarcoid group [12] and to tuberculosis papulonecrotica,[13] the histologic observations, the positive anergy and the occurrence of mottling of the lungs are arguments for those who assume its tuber-

TABLE 4.—*Tuberculin-Sensitivity in Patients with Sarcoidosis and Granuloma Annulare* *

Diagnosis	Sex	Number of Patients	Average Age, Years	Old Tuberculin, Dilution of 1:5,000			
				Positive Results		Negative Results	
				Number	Per Cent	Number	Per Cent
Sarcoidosis (lymphogranulomatosis benigna, sarcoid Boeck and lupus pernio)	Total	22	42	11	50.0	11	50.0
	Male	9	43	4	44.4	5	55.6
	Female	13	42	7	53.6	6	46.2
Granuloma annulare	Total	14	24	6	42.9	8	57.1
	Male	4	21	1	25.0	3	75.0
	Female	10	26	5	50.0	5	50.0

* These cases are identical with those in table 1, but records of only 22, 14 and 19 cases, respectively, were available.

TABLE 5.—*Occurrence of Osteitis Cystica Multiplex in Patients with Sarcoidosis* *

Sex	Number of Patients	Average Age, Years	Osteitis Cystica Occurred in		
			Tuberculin-Positive Patients	Tuberculin-Negative Patients	Total
Total	19	40	1	6	7
Male	7	42	..	3	3
Female	12	38	1	3	4

* These cases are identical with those in table 1, but records of only 22, 14 and 19 cases, respectively, were available.

culous origin. But this theory is far from being generally accepted. My statistics are not conclusive. They may be compared with the figures

10. (*a*) Jacobi, F.: Granuloma annulare, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 10, pt. 1, pp. 796-822. (*b*) Michael, J. C.: Etiology of Granuloma Annulare, with Special Reference to the Tuberculous Theory, Arch. Dermat. & Syph. **29**:189-205 (Feb.) 1934. (*c*) Goodman, M. H., and Ketron, L. W.: Granuloma Annulare: Report of Unusual Cases with Comments on the Histology of the Disease, ibid. **33**:473-494 (March) 1936. (*d*) Fellner.[2d]

11. Halliwell, E. O., and Ingram, J. T.: Granuloma Annulare, Brit. J. Dermat. **47**:319-340, 1935.

12. Martenstein, H., and Noll, R.: Statistische Untersuchungen über die Tuberkulinreaktion, Arch. f. Dermat. u. Syph. **158**:409-420, 1929.

13. Pinkus, H.: Ueber atypische Tuberkulide, zugleich ein Beitrag zur Ätiologie des Granuloma annulare, Arch. f. Dermat. u. Syph. **170**:194-222, 1934.

compiled by Michael [10b] from 50 cases in the literature; he found no tuberculosis in 70 per cent, healed tuberculous lesions in 4 per cent, questionable changes in 10 per cent and active tuberculosis in 16 per cent.

Table 4 shows the high incidence of negative reactions to tuberculin, which is in agreement with other statistics.[14] The age may partly account for these results, the average age of those with negative reactions being 18 (5 to 36), as compared with 32 (18 to 49) in the group with positive reactions.

Lupus Erythematosus.—The discussion of the cause of lupus erythematosus is still a favorite topic of dermatologic meetings.[15] The tuberculous origin (Besnier) of this disease, as assumed by the French and part of the Austrian, German and Swiss schools, has never appealed greatly to the American and British dermatologists.[16] Numerous studies have been devoted in recent years to the relation between lupus erythematosus and tuberculosis; [17] the tuberculous theory still has its supporters [18]

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14. Martenstein and Noll.[12] Michael.[10b]

15. (*a*) Belote, G. H., and Ratner, H. S. V.: The So-Called Libman-Sacks Syndrome: Its Relation to Dermatology, Arch. Dermat. & Syph. **33**:642-664 (April) 1936. (*b*) Engman, M. F., Jr.: Early Acute Lupus Erythematosus, ibid. **35**:685-697 (April) 1937. (*c*) Mook, W. H.; Weiss, R. S., and Bromberg, L. K.: Lupus Erythematosus Disseminatus, ibid. **24**:786-829 (Nov.) 1931. (*d*) Séance spéciale du 14 mai 1939, consacré au lupus érythémateux: Etiologie. Pathogénie, Bull. Soc. franç. de dermat. et syph. **46**:1030-1177, 1939.

16. (*a*) Macleod, J. M. H.: Lupus Erythematosus: Some Observations on Its Etiology, Arch. Dermat. & Syph. **9**:1-12 (Jan.) 1924. (*b*) Montgomery, H.: Disseminate Lupus Erythematosus as a Systemic Disease, in Christian, H. A.: Oxford Medicine, New York, Oxford University Press, 1939, vol. 4.

17. (*a*) Cannon, A. B., and Ornstein, G. G.: The Tubercle Bacillus as an Etiologic Factor in Lupus Erythematosus, Arch. Dermat. & Syph. **12**:691 (Nov.) 1925. (*b*) Ehrmann, S., and Falkenstein, F.: Ueber Lupus erythematodes, Arch. f. Dermat. u. Syph. **141**:408-506, 1922. (*c*) Keil, H.: Relationship Between Lupus Erythematosus and Tuberculosis: A Critical Review Based on Observation at Necropsy, Arch. Dermat. & Syph. **28**:765-779 (Dec.) 1933. (*d*) Pautrier, L. M.: Lupus érythémateux, in Darier, J., and others: Pratique nouvelle dermatologique, Paris, Masson & Cie, 1936, vol. 3, pp. 733-824. (*e*) Ramel, E.: Neuere Beobachtungen und Anschauungen über die Beziehungen des Lupus erythematodes zur Tuberkulose, Med. Klin. (Extrapulmonale Tuberkulose supp. 3), 1925, pp. 11-24. (*f*) Throne, B.: Lupus Erythematosus: A Clinical Study, Arch. Dermat. & Syph. **12**:33-40 (July) 1925. (*g*) Symposium: Was spricht für und gegen die tuberkulöse Natur des Lupus erythematodes? Dermat. Wchnschr. **99**:1346-1356, 1934. (*h*) Veiel, F.: Lupus erythematodes, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 10, pt. 1, pp. 687-795. (*i*) Weidman, D., and Gilman, R. L.: A Case of Acute Disseminated Lupus Erythematosus: Necropsy Disclosing Acute Endocarditis but Not Tuberculosis, Brit. J. Dermat. **43**:641-647, 1931. (*j*) Macleod.[16a]

18. Stokes, J. H., in discussion on Engman.[15b] Cannon and Ornstein.[17a] Ehrmann and Falkenstein.[17b] Marchionini.[15d] Ramel.[15d]

but is losing ground.[19] At present the majority apparently consider lupus erythematosus either to be a syndrome (Jadassohn) caused by various agents, such as infections, drugs [20] or mineral poisons [21]—in other words, a "reaction cutanée" (Brocq) "based on a certain form of immunologic response" [20]—or a clinical entity of its own, caused either by a known agent, such as the streptococcus [22] or a focal infection,[23] or by an unknown organism.[24]

The association of pulmonary tuberculosis and lupus erythematosus has been a subject of wide controversy. The literature lists positive findings from 5 per cent [16] to 100 per cent.[25] Differences of methods, small numbers of cases, lack of comparison with adequate controls and other factors, such as different incidence of tuberculosis in various countries and errors in diagnosis, may account partly for these discrepancies. They render the comparison and evaluation of these statistics difficult if not impossible.

My statistics of 211 cases constitute–so far as I can see–the largest single report on this subject. The results are based exclusively on roentgenologic examinations of the lungs; other forms of tuberculosis, such as involvement of the lymph nodes, have not been considered. The incidence of active tuberculosis (7.2 per cent) is decidedly lower than average in persons with true tuberculosis of the skin or in any single group of patients with this condition large enough for comparison (table 2). On the other hand, the percentage is higher than average among syphilitic patients but is not far above the figure found in patients with neurosyphilis (6.7 per cent). If one considers the figures of inactive tuberculosis, those of lupus erythematosus (46.8 per cent) rank closer to those of cutaneous tuberculosis (51.2 per cent) than to those of syphilis (32.6 per cent); however, the comparison with the syphilitic

19. Cummer, C. L.: Etiology of Lupus Erythematosus: Occurrence in the Negro, Arch. Dermat. & Syph. **33**:434-445 (March) 1936. Belote.[3b] Keil.[17c]

20. Sulzberger, M. B., in discussion on Engman.[15b] Rost.[15d]

21. Ludy, J. B., and Carson, E. F.: Lupus Erythematosus: Increased Incidence, Hematoporphyrinuria and Spectroscopic Findings, Arch. Dermat. & Syph. **35**:403-416 (March) 1937.

22. Barber, H. W.: A Case of Lupus Erythematosus Associated with Streptococcal Infection of the Tonsils, Brit. J. Dermat. **31**:186-193, 1919; cited by Ramel.[17e] O'Leary, P. A., in discussion on Engman,[15b] and on Mook.[15c]

23. Tolman, M. M., in discussion on Ludy and Carson.[21] Ayres, S., Jr., in discussion on Mook.[15c] Throne.[17f]

24. Lindenberg, A.: Contribuição ao estudio da etiologia do lupus erythematosa, Arch. de dermat. et syph. de São Paulo **1**:147-149, 1937; abstracted, Zentralbl. f. Haut- u. Geschlechtskr. **59**:307, 1938. Belote.[3b]

25. Kren, O.: Zur Klärung der Pathogenese des Lupus erythematosus acutus, Wien. med. Wchnschr. **86**:680-683, 1936; abstracted, Wise, F., and Sulzberger, M. B.: Yearbook of Dermatology and Syphilology, Chicago, Year Book Publishers, Inc., 1937, pp. 224-225. Ehrmann and Falkenstein.[17b]

controls is somewhat hampered in group 1 by the previously mentioned fact that they were primarily examined on account of the heart and aorta.

My results agree with those of others.[26] I do not think that these statistics can be used to support the tuberculous theory.

INCIDENCE OF TUBERCULOSIS OF THE LUNGS IN PATIENTS WITH TRUE TUBERCULOSIS OF THE SKIN

Three facts seem noteworthy:

1. The occurrence of active tuberculosis of the lungs in patients with different types of cutaneous tuberculosis shows great variations, being highest in patients with tuberculosis verrucosa and lowest in patients with the lupus miliaris-rosacea-like tuberculid group of conditions.

2. The incidence of progressive pulmonary tuberculosis in patients with lupus vulgaris as found in my series agrees well with other statistics.[27] The fact that 16 per cent of these patients exhibited signs of active tuberculosis of the lungs seems to contradict the general belief [28] that the combination of lupus vulgaris and active tuberculosis is unusual. Apparently, there are two different problems: lupus vulgaris as a complication of tuberculosis of the lungs is exceedingly rare; the opposite, however, pulmonary tuberculosis as a complication of lupus vulgaris, is not so unusual. Of course, this becomes more evident when a larger series such as mine is studied over a period of many years.

3. Men and women with lupus vulgaris show the same incidence of all types of pulmonary conditions. This is in contradistinction to some previous statistics [27] based on a smaller amount of material.

INCIDENCE OF TUBERCULOSIS OF THE LUNGS IN PATIENTS WITH DIFFERENT STAGES OF SYPHILIS

The incidence of tuberculosis of the lungs is slightly higher in patients with late stages of syphilis than in those with early stages. It remains

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26. Goeckerman, W. H.: Is Lupus Erythematosus Discoides Chronicus Due to Tuberculosis? Arch. Dermat. & Syph. **3**:788-801 (June) 1921. Pautrier and Schaaff.[15d]

27. (*a*) Martenstein, H.: Die Lungentuberkulose als Komplikation der Tuberkuloderme, Arch. f. Dermat. u. Syph. **131**:168-179, 1921; (*b*) Weitere Mitteilung über die Lungentuberkulose bei Tuberkulodermen, ibid. **140**:341-345, 1922. (*c*) Memmesheimer, A. M.: Untersuchungen über den Einfluss des Hauttuberkulose auf die Lungentuberkulose, ibid. **174**:511-517, 1936. (*d*) Schmitt, K.: Hauttuberkulose und Lungentuberkulose, Strahlentherapie **63**:52-56, 1938.

28. Fox, H.: Lupus Vulgaris and Pulmonary Tuberculosis, Arch. Dermat. & Syph. **40**:154-155 (July) 1939. Cannon, B. A.; Combes, F. C., and MacKee, G. M., in discussion on Fox.

an open question whether this fact—if not altogether incidental—is due to differences of age or whether it reflects an influence of the existing syphilis.

SUMMARY

Statistics concerning the incidence of tuberculosis of the lungs in 28 patients with sarcoidosis (lymphogranulomatosis benigna, Besnier-Boeck-Schaumann disease, sarcoid of Boeck, lupus pernio), in 23 patients with granuloma annulare and in 211 patients with lupus erythematosus are presented and compared with analogous statistics of 1,028 cases of ascertained tuberculosis of the skin and 2,484 cases of syphilis.

Sensitivity to tuberculin in patients with sarcoidosis and granuloma annulare and occurrence of osteitis tuberculosa multiplex cystoides (Jüngling) in sarcoidosis are reported.

EARLY SYPHILITIC LESIONS MISTAKEN FOR DERMATOPHYTOSIS

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AND
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Among the commonest lesions of secondary syphilis are moist papules, which are usually found about the genitals and anus. When fused in plaques they form the familiar condylomata lata of secondary syphilis, and it has long been known that their growth is favored by the moisture, heat and friction of opposing surfaces.

One of the less common places for such lesions, and one that may be overlooked and thus cause an error in diagnosis, is between the toes, especially if the patient has an associated dermatophytosis. In our experience it is not uncommon to see patients who have attended clinics and have been treated for dermatophytosis when there was an associated syphilitic process present. The moist, boggy skin with macerated opposing surfaces that characterizes fungous infections between the toes offers an ideal place for the localization of Spirochaeta pallida and the formation of moist papules, which in some cases present the typical picture of condylomata lata. Ch'in [1] reported 3 such cases in Shanghai in 1932, but, so far as we know, similar reports from this country have been extremely rare.

At Bellevue Hospital secondary syphilitic lesions between the toes have been noted a number of times. Between September 1938 and February 1940, 6 cases were observed, and in 5 of these treatment had been given for varying lengths of time for stubborn dermatophytosis. When the lesions failed to respond to the usual treatments with potassium permanganate and compound ointment of benzoic acid U.S.P., the patients were referred to the dermatologic wards, where the presence of early syphilis was diagnosed and confirmed in every case by the finding of S. pallida on dark field examination. In each patient spirochetes were found in serum taken from lesions between the toes. Dark

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1. Ch'in, T. L.: Syphilis of Toes Resembling Fungus Infection (Hongkong Foot): Report of Three Cases, Chinese M. J. **46**:60-63 (Jan.) 1932.

field examination of fluids taken from the lesions of dermatophytosis in patients without early syphilis have never shown similar spirochetes in our experience. In addition, all of the patients in whom S. pallida was found had strongly positive Wassermann reactions of the blood.

In 4 of the 6 cases the diagnosis of early syphilis could have been made from other clinical manifestations of the disease besides the lesions between the toes. Failure to strip the patients or to elicit an adequate history was solely responsible for the delay in diagnosis. One gave a history of sores about the anus of three months' duration and foul-smelling sores between the toes for about the same period. At the time of examination he had, in addition to the lesions about the anus and between the toes, flat papules on the shaft of the penis and a sore throat. Two patients had primary lesions on the penis as well as scrotal lesions and scattered papules on the trunk and extremities, including the palms and soles in 1 case. All had dermatophytosis, and all but 1 had been treated for this condition after the appearance of early syphilitic lesions. In 3 cases the condition was less easily diagnosed, and these merit more detailed report.

REPORT OF CASES

CASE 1.—*Probable chancre between the toes.*

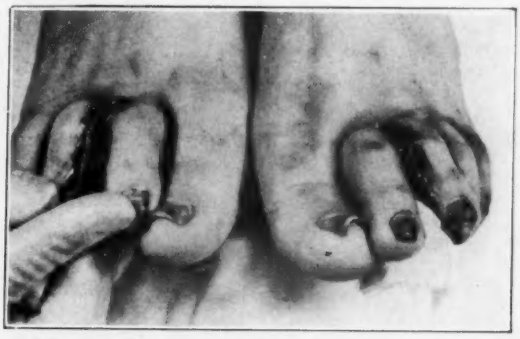
A Negro aged 20 was admitted to the wards of Bellevue Hospital on Sept. 12, 1938. He gave a history of "ringworm" between the toes of both feet of over one year's duration. Examination revealed the characteristic lesions of dermatophytosis on both feet, but in addition between the fourth and fifth toes of his right foot he had a single, deep ulceration. The ulcer was well demarcated, indurated and covered by a rather firm necrotic callus. The surrounding skin showed considerable maceration. He had bilateral discrete, nontender inguinal nodes and a single large, visible node in the right femoral region. This was considered a satellite bubo, in view of the other findings. There were no other cutaneous lesions, but the patient had a red throat and hypertrophied tonsils. The Wassermann reaction of the blood was strongly positive, and dark field examination of the ulcer between the toes revealed spirochetes typical of S. pallida. From the history obtained this ulcer had started about ten weeks prior to admission and had been treated locally as dermatophytosis.

Within two weeks after the starting of antisyphilitic treatment with arsphenamine the ulcer was entirely healed, though the dermatophytosis remained. The femoral node had become reduced in size during the same period. The diagnosis of chancre seemed justified in this case, though nothing could be elicited from the patient's history as to how he contracted a primary syphilitic lesion in so unusual a place.

CASE 2.—*Prolonged duration of moist papules between the toes.*

A white man aged 34 was admitted to one of the surgical wards of Bellevue Hospital on Nov. 16, 1939, because of ulcerations between the toes, which had become so painful that he had been unable to walk for the previous six weeks. During this time he stated that he had lost 10 pounds (4.5 Kg.) in weight. He was transferred to the dermatologic wards of the hospital, with a diagnosis of dermatophytosis and probable syphilis. Apart from the history of the condition

of his feet the patient volunteered no information, and such data as could be obtained may not have been entirely accurate. Repeated questioning, however, elicited consistent answers regarding previous genital lesions. He maintained that he had first noticed an ulcer on the penis some time in February 1939. He was not sure how long this lasted, but apparently its duration was at least two months. Some time in March, about two months prior to the appearance of papules on the genitalia, he first noted sores between his toes. As nearly as he could recall, in May a sore throat developed and he noted red papules on the shaft of his penis and scrotum. He was again vague about the duration of these lesions but was sure they had not been present for at least two months prior to admission. He stated that he had been treated intermittently for "athlete's foot" for six or seven months prior to admission to Bellevue Hospital and that he had been annoyed by the foul odor of his feet during that time. The sores, however, had become decidedly painful only about two months prior to admission, after the use of a "potash solution" locally. The odor had become even more offensive during this period.



Secondary syphilitic lesions mistaken for dermatophytosis.

On examination the scar of the penile lesion which had started nine months prior to admission was still plainly visible. No other lesions could be found about the genitals or anus. He had no cutaneous manifestations apart from those between the toes. The photograph was taken after much of the superficial debris had been removed and most of the edema had subsided. Beneath the crusts typical small condylomata lata were visible between all of the toes. Numerous spirochetes were seen on dark field examination of the fluid oozing from the lesions. They had the typical appearance of S. pallida, and the Wassermann reaction of the patient's blood was strongly positive. In addition he had a red throat with small papules on the anterior pillars, that disappeared entirely after one injection of mapharsen. He stated that he did not have a sore throat at the time of admission but that his throat had been sore for some months prior to admission. Within a week after the first injection of mapharsen there was great improvement of the lesions between the toes, and within two weeks they were entirely healed except for the evidences of persisting fungous infection. The throat cleared within four days aftr treatment was started.

If the patient's history can be believed, this case is an unusual one of secondary syphilitic lesions persisting for months between the toes and probably in the throat long after other secondary manifestations had disappeared. We have observed cases of early syphilis in which sore throats remained for weeks after the cutaneous

lesions had disappeared, but in this patient moist papules continued between the toes for at least two months after they had entirely disappeared from the genitals. The trauma of walking, local treatments and the associated dermatophytosis between the toes evidently favor the prolonged continuation of moist papules with active spirochetes after the skin elsewhere has become resistant to the presence of spirochetes.

CASE 3.—*Relapsing secondary syphilis with moist papules between the toes.*

A white man aged 26 was admitted to the dermatologic wards of Bellevue Hospital on Feb. 27, 1940, because of foul-smelling sores between the toes of both feet and large fleshy papules on his scrotum. He gave a history of having had a chancre on the penis in December 1935, at which time he attended a department of health clinic. A report of the findings at that time, obtained from the clinic, included the facts that S. pallida was found in the chancre and that the Wassermann reaction of his blood was strongly positive. Between December 1935 and June 1936 he received fourteen injections of mapharsen and three injections of a bismuth compound, irregularly spaced. He had no treatment after that. About Jan. 25, 1940, he noticed papules on his scrotum and sores between his toes. He had had "athlete's foot" for several months prior to this date and went to a clinic because of his feet. A routine Wassermann test of the blood gave a positive result, and his scrotal lesions were then discovered. S. pallida was found on dark field examination of the sores between the toes. The unusual feature of this case was the four year interval between his initial lesion and the relapsing secondary manifestations.

SUMMARY AND CONCLUSIONS

Dermatophytosis between the toes provides a favorable soil for the localization and growth of S. pallida, with the formation of infectious early syphilitic lesions.

Six cases of such a condition are reported, in 1 of which the lesion was probably a chancre.

Moist papules between the toes, like lesions in the throat, may persist after all other cutaneous lesions have disappeared.

TURBAN TUMORS

REPORT OF A CASE WITH UNUSUAL PATHOLOGIC FINDINGS, INCLUDING BOTH EPIDERMAL AND DERMAL NEVI

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Congenital and acquired multiple tumors of the scalp are infrequently reported in the literature. They have been described by different authors under many titles, such as turban tumor, naevo-epithelioma adenoides, cylindroma, multiple benign epithelioma, fibroma multiplex, sarcoma capitis, endothelioma capitis and sweat gland carcinoma. The diversity of names resulted from the variation of histologic observations and interpretations made by past investigators.

In 1841 Ancell [1] described a case of tumors of the scalp. Baker, Kaposi and Orro,[2] as well as Poncet [3] and Cohn,[4] considered the condition some form of sarcoma. Spiegler [5] concluded that the growths in the cases of Ancell, Kaposi, Poncet and Cohn were endotheliomas, not sarcomas. An example of endothelioma of the scalp had been presented by Mulert [6] two years previously. The differentiating feature observed in the descriptions of Baker, Kaposi and Orro was a history of trauma preceding the development of the tumors.

About the same time Barrett [7] published a report of a mother and 2 daughters all with similar lesions, to which he attached the name

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From the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, Columbia University.

1. Ancell, H.: History of a Remarkable Case of Tumours, Developed on the Head and Face, Accompanied with a Similar Disease in the Abdomen, M. Chir. Tr. **25**:227, 1842; reviewed, Arch. Surg. **6**:119, 1895.

2. Cited by Crocker, H. R.: Diseases of the Skin, ed. 3, Philadelphia, P. Blakiston's Son & Co., 1903, p. 1027.

3. Poncet, A.: Note sur une variété de tumeurs confluentes du cuir chevelu, Rev. de chir., Paris **10**:244, 1890.

4. Cohn, I. E.: Multiple Sarcoma of the Scalp, J. Cutan. Dis. **10**:398, 1892.

5. Spiegler, E.: Ueber Endotheliome der Haut, Arch. f. Dermat. u. Syph. **50**:163, 1899.

6. Mulert, D.: Ein Fall von Multiplen Endotheliomen der Kopfhaut, Arch. f. klin. Chir. **54**:658, 1897.

7. Barrett, J. W., and Webster, P.: Multiple Sudoriparous Adenomata Occurring on the Scalp and Face in Three Members of the Same Family, Brit. M. J. **1**:272, 1892.

multiple sudoriparous adenomas. Later Fick [8] denouced the term endothelioma, and Frieboes [9] concluded that most of these conditions were examples of epithelial tumors of slow growth. Cylindroma, a substitute term for endothelioma, originated with Billroth,[10] and many examples of this are to be found in the literature. Jones, Alden and Bishop [11] described their case as one of sweat gland carcinoma of low grade malignancy.

Stillians,[12] in his series of cases, concluded that cylindromas are basal cell epitheliomas which may originate from the surface epithelium or the hair follicle. He preferred the name naevo-epithelioma adenoides, suggested by Hoffman.[13] Zakon [14] also reported a case under this heading. Binkley,[15] in describing his series, slightly altered this name, to naevus epitheliomato-cylindromatosus.

Jones, Alden and Bishop, Stillians and Binkley, in their respective articles, have thoroughly reviewed the literature to the present, including the earliest cases, occurring in the middle of the last century. In contrast, our case of turban tumor does not present the same features as those heretofore described.

REPORT OF CASE

History.—L. W., a Negro aged 19, was admitted to the Medical Center of Jersey City in March 1931, with pneumonia. An uneventful recovery followed. Coincidentally, he presented multiple tumors on the right side of his scalp. The patient stated that all the growths had been present since birth, and none had spontaneously appeared or disappeared thereafter. They enlarged in proportion with the growth of his head. There were never any subjective symptoms or any bleeding, oozing, ulcerations or infections. Several physicians at various times advised against therapeutic intervention.

The family history was irrelevant and no member had any similar condition.

Physical Examination.—Covering the right parietal and occipital regions of the scalp and extending medially to about 1 inch (2.5 cm.) of the midline and laterally to about 1 inch above the lobe of the ear were numerous tumor masses

8. Fick, J.: The Impracticability of "Endothelioma" as a Working Hypothesis, J. Cutan. Dis. **50**:444, 1912.

9. Frieboes, W.: Beitrag zur Klinik und Histopathologie der gutartigen Hautepitheliome, Berlin, S. Karger, 1912.

10. Cited by Dalous, E.: Le cylindrome de la peau, Arch. de méd. expér. et d'anat. path. **15**:796, 1903.

11. Jones, J. W.; Alden, H. S., and Bishop, E. L.: Turban Tumor, or Sweat Gland Carcinoma, Arch. Dermat. & Syph. **26**:656 (Oct.) 1932.

12. Stillians, A. W.: Nevo-Epithelioma Adenoides (Cylindroma) of the Scalp, Arch. Dermat. & Syph. **26**:481 (March) 1933.

13. Hoffman, E., cited by Gans, O.: Histologie der Hautkrankheiten, Berlin, Julius Springer, 1928, vol. 2, p. 297.

14. Zakon, S. J.: Naevo-Epithelioma Adenoides (Cylindroma) of the Scalp, Arch. Dermat. & Syph. **40**:945 (Dec.) 1939.

15. Binkley, G. W.: Naevus Epitheliomato-Cylindromatosus, Arch. Dermat. & Syph. **37**:289 (Feb.) 1938.

(approximately a hundred). These varied from 3 mm. to 3 cm. in diameter, the average being about 1 cm. Over the parietal area the lesions were comparatively small, the largest being about 1.5 cm. These were closely massed; most of them were pedunculated, and some were fused together. The tumors could be separated easily, thereby revealing their point of attachment to the scalp. They appeared not unlike the cerebral convolutions. Over the anterior occipital region the growths were more uniform in size, varying from 0.25 to 0.75 cm. in diameter; they were fewer, and they arose directly from the scalp. The largest lesion, located in the posterior occipital region, was attached to the scalp by a pedicle 0.5 cm. in diameter. The mass overhung the upper part of the neck. Two smaller masses arose from the upper and lower poles of this larger one, the former 1 cm. and the latter 1.5 cm. in diameter.

Fig. 1.—Turban tumor in a Negro aged 19.

The tumors were mostly spherical, although some were pear shaped (like the largest one) and others were flat. They ranged from light brown to almost black, the surface being lighter than parts nearer the scalp. The surface was glistening, tense, firm and smooth except in a few pitted zones. The lesions themselves were entirely devoid of hair; however, the hair between the lesions was like that on the rest of the scalp.

The individual tumors were not movable on the deeper parts, but the entire area containing the tumors and the underlying scalp were easily raised off the skull. This area of the scalp appeared to be more loosely attached to the skull than the rest.

Otherwise, physical examination of the patient revealed no abnormalities. A roentgenogram of the skull was normal. The Wassermann reaction of the blood was negative.

Histologic Examination.—The section was large and round and was covered by epidermis except at its base. In part the epidermis was thin and flattened, and in part it was thickened; and in the latter areas the cells were arranged in bands and strands, some of which anastomosed to form a coarse network (fig. 2). For the greater part, the basal cell margin was uniform, orderly and intact. However, in some areas there were small nests of epithelial cells in the basal cell margin (fig. 2). Where epidermis was thin and flattened there were no rete pegs and papillary bodies.

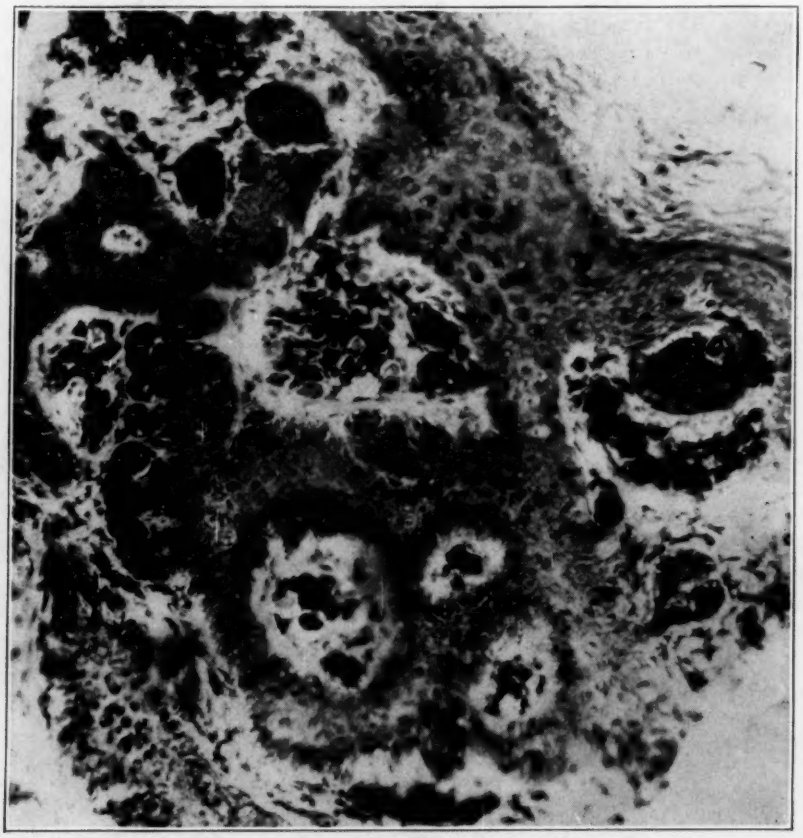

Fig. 2.—An intraepidermal nevus and a junction type nevus (high power).

Throughout the midcutis there was in bandlike fashion a mass of cells (considered by many to be of epithelial origin), some arranged in groups and some isolated (fig. 3). The entire upper part of the cutis was free of these cells. With high power these cells were seen to have large round hyperchromatic nuclei and definite lightly stained cell bodies. In places the cell outlines were easily distinguished. Many of the cells were multinucleated. There was a small amount of pigment present in and about these cells. The nuclei of all the cells were fairly uniform in size and shape. The nests of cells in the lower border of the epidermis were composed of cells of a similar nature.

The entire connective tissue framework was moderately increased, in some areas taking on a whorl formation (fig. 4). In some regions there were numerous dilated thin-walled blood vessels, some of which were filled with blood elements

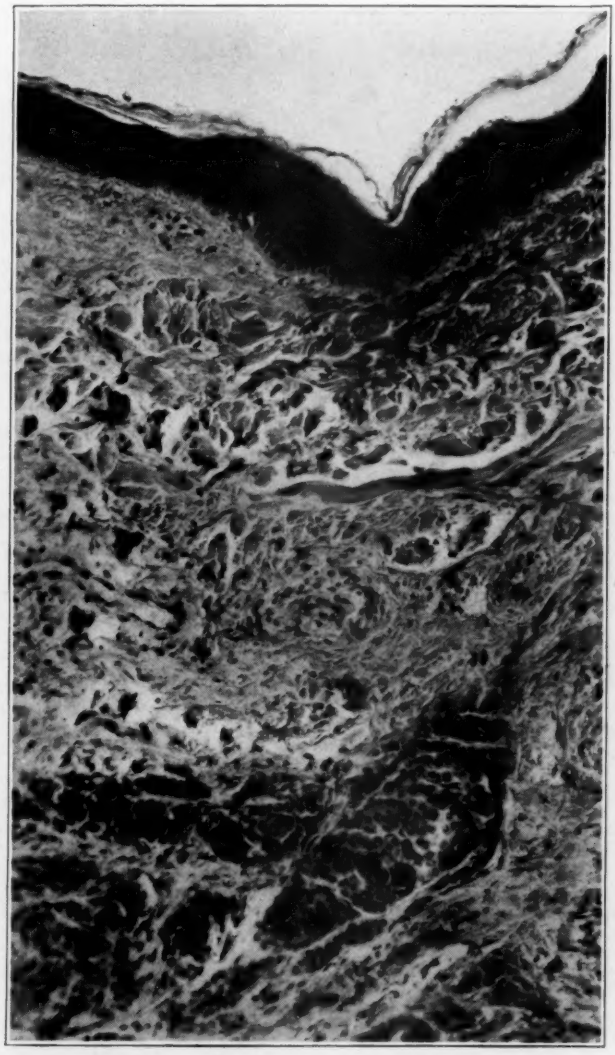

Fig. 3.—An intradermal cellular nevus (low power).

(fig. 5). Nowhere in the section was there any inflammatory process. Hair follicles or sebaceous glands were not present.

Throughout the entire cutis framework there was sparse diffuse infiltrate composed of spindle cells and fibroblasts.

The entire tissue was an example of a congenital malformation consisting of a hyperplastic intraepidermal cellular nevus, a junction type nevus, an intradermal cellular nevus (origin of the two latter is still a matter of dispute) and also the mesenchymal process, such as the fibromatous nevus within which was an angioma. The entire picture fit in with a mixed nevus.

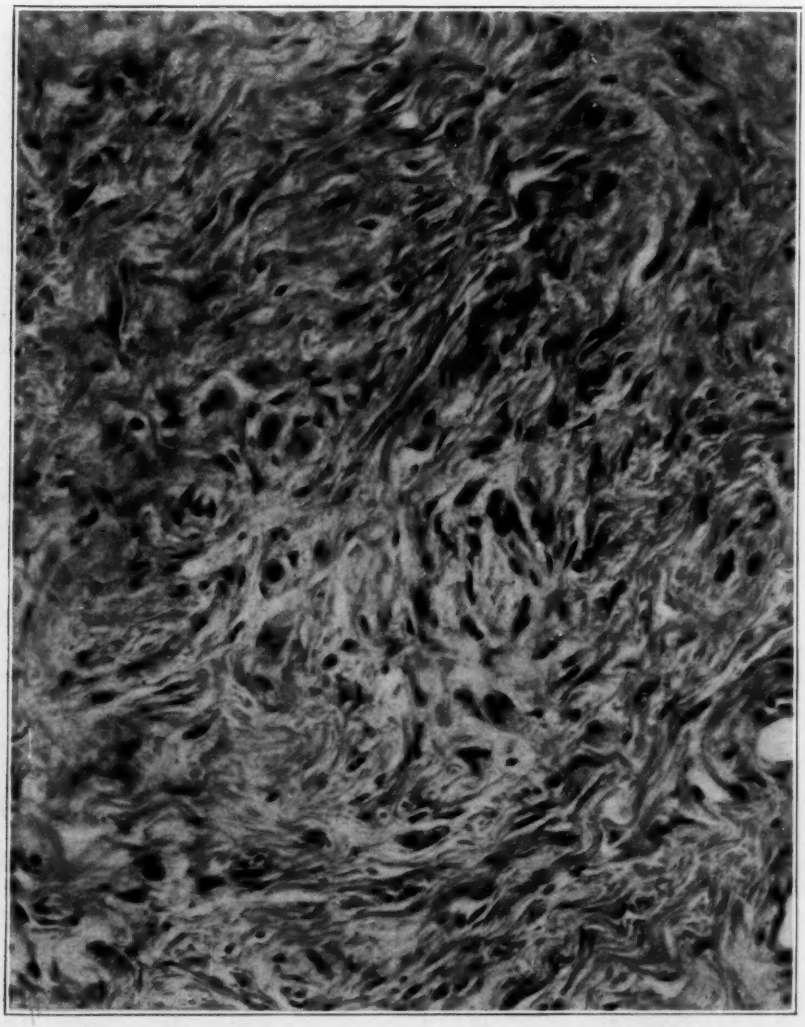

Fig. 4.—A fibromatous nevus (high power).

COMMENT

Obviously, turban tumor is not a histologic entity but a clinical term. Microscopic study is necessary for the more accurate diagnosis. Our case shows the clinical features seen in turban tumors; however, the histologic features are not in accord with those previously reported.

The only case similar to ours was mentioned by Binkley. Clinically the tumor in his case was called a cylindroma; it grew rapidly and metastasized after injury. At postmortem examination the diagnosis of nevocarcinoma was made. Binkley inferred from this that any tumors of the scalp accompanied by rapid growth and metastasis should not be called turban tumor. Furthermore, this author claimed that malignant tumors of the scalp, unless originating from the benign basal

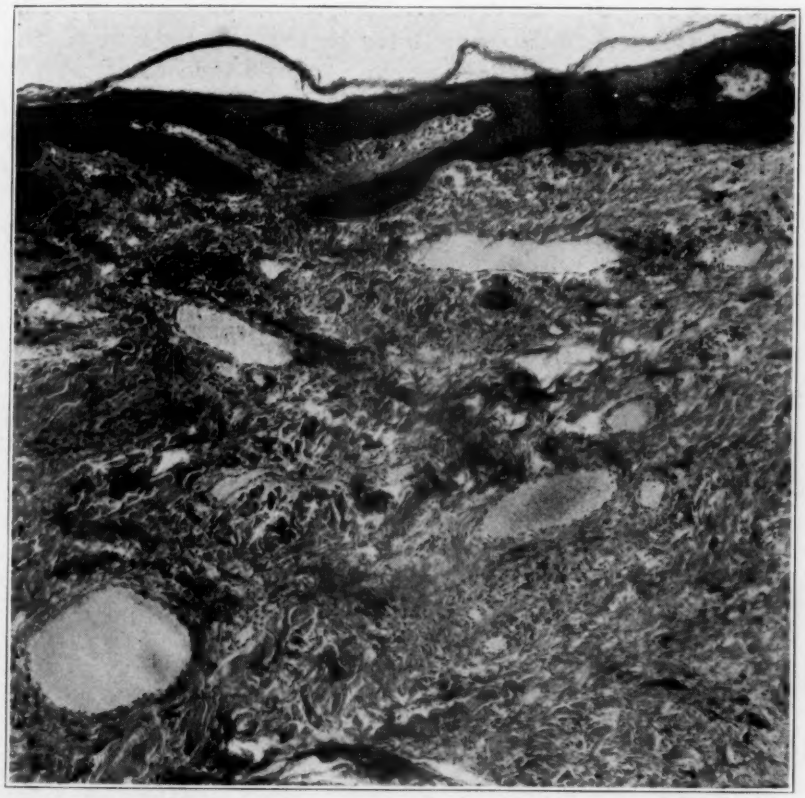

Fig. 5.—An angioma (low power).

cells of a typical cylindroma, should not be included in this classification. We cannot fully agree with this; although the condition in our case was shown to be not a cylindroma on microscopic examination, its clinical picture was indistinguishable from that seen in the condition. As in our case, in which the growth would also be a nevocarcinoma if a malignant change should occur (malignant development of the junction type nevus), the diagnosis was turban tumor until microscopic examination revealed the true nature of the dermatosis.

In most of the cited cases, the tumors seem to be of nevoid origin. This observation also was made by Stillians. In discussing this article, McCarthy corroborated this view, and Weidman furthermore maintained the possible derivation from the skin plate of Remak (an embryologic structure).

Depending on the stage of development the tumors may apparently arise from the epidermis, the sweat glands or the pilosebaceous apparatus. Ronchese [16] was in accord with this view and furthermore suggested that the most probable derivation was from the sebaceous glands. Sutton and Sutton [17] discussed turban tumors under the heading of syringoma but stated the opinion that the origin need not necessarily be from the sweat apparatus but may be from other epithelial structures. In our case, since the tumors were present at birth and the microscopic picture is that of a nevus (mixed), the nature of the dermatosis is evident.

Clinically these cases closely resemble each other, with slight variations. Some had single lesions; others, multiple. Often heredity seemed to play an important role, when many members of a family were similarly afflicted. Greater incidence is found among females. At times, in conjunction with the tumors of the scalp, lesions of the face and of the trunk were present. In the reports of Watanabe,[18] Schlammadinger,[19] Biberstein [20] and others, these tumors proved to be of the trichoepithelioma group.

SUMMARY

The first case of turban tumor in a Negro is reported.

The tumors were present at birth and were confined to the scalp.

The lesions were of mixed, epidermal and dermal types.

Turban tumor is a descriptive clinical term, and in each case histologic study is necessary for diagnosis of the type of nevus.

Dr. David L. Satenstein gave assistance in the preparation of this paper.

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57 West Fifty-Seventh Street, New York.

16. Ronchese, F.: Multiple Benign Epithelioma of the Scalp (Turban-Tumors), Am. J. Cancer **18**:875, 1933.

17. Sutton, R. L., and Sutton, R. L., Jr.: Diseases of the Skin, ed. 10, St. Louis, C. V. Mosby Company, 1939.

18. Watanabe, J.: Ueber das Cylindrom und das Epithelioma adenoides cysticum, Arch. f. Dermat. u. Syph. **140**:208, 1922.

19. Schlammadinger, J.: Cylindrom und Trichoepithelioma papulosum multiplex, Arch. f. Dermat. u. Syph. **171**:526, 1935.

20. Biberstein, H.: Epithelioma adenoides cysticum im Gesicht und Cylindrom am Kopf, Arch. f. Dermat. u. Syph. **142**:428, 1923.

VAGINAL MELANOSIS CAUSED BY BISMUTH THERAPY AND CARCINOMA OF THE CERVIX

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Discoloration of the skin or mucosa after bismuth medication is known to occur in three forms.

1. A general discoloration may be caused by deposits of metallic bismuth in the entire skin, particularly of the face and hands. This extremely rare condition resembles argyria. Lueth, Sutton, McMullen and Muehlberger [1] described and showed a colored picture of a man who for the treatment of a gastric condition took bismuth compounds internally over a long period. He had also taken silver nitrate before. Within a relatively short time his face and hands became deep blue-black, and the covered parts of the body became ashen gray. As in argyria, the discoloration persisted. Chemical analysis of a piece of skin (2 by 4.5 cm.) ruled out silver and other metals and gave positive reactions for bismuth. Many small deposits of bismuth were seen in the microscopic sections. Small granules were evenly scattered throughout the corium. Considering the tremendous number of patients treated with bismuth over long periods and the extreme rarity of "bismuthia," one cannot help thinking that one or several unknown factors are essential to produce this spectacular result.

2. Rarely a discoloration follows accidental injection of a bismuth preparation into an artery. There the bismuth salts travel as emboli with the blood stream to the muscles and to the skin, producing acute severe pain and inflammatory reactions, ranging from slight irritation to deep and wide necroses. Most often swelling and purple or bluish net-shaped areas of discoloration are seen. The condition heals, leaving long-lasting pigmentation. Freudenthal,[2] who in 1924 described the local embolic exanthema due to bismuth, showed in histologic sections that the small arteries in the lesions were filled with crystals identical with those used in the emulsion.

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1. Lueth, H. C.; Sutton, D. C.; McMullen, C. J., and Muehlberger, C. W.: Generalized Discoloration of Skin Resembling Argyria Following Prolonged Oral Use of Bismuth: Case of "Bismuthia," Arch. Int. Med. **57**:1115 (June) 1936.

2. Freudenthal, W.: Lokales embolisches Bismogenol-Exanthem, Arch. f. Dermat. u. Syph. **147**:155, 1924.

3. The third type of discoloration caused by bismuth is the black deposit of bismuth sulfide. This is the most common form. It has been seen by some authors in more than 90 per cent of the patients treated with injections of a bismuth salt as a narrow gray, blue or black line along the edges of the gums. It appears most frequently in connection with tartar. It is more pronounced on the dental side of the gums than on the buccal side. It usually starts in, and is often confined to, the region of the incisor teeth.

The gum line persists for months after discontinuation of the treatment. In a small number of cases ulcerative or gangrenous stomatitis follows the appearance of the gum line. Oral sepsis and use of soluble bismuth salts accelerate the production of the deposits, which rarely appear in children, in women during the second half of pregnancy (Löhe and Rosenfeld [3]) or in edentulous mouths (McCarthy and Dexter [4]). Bismuth melanosis of the tongue and of the buccal mucosa is a warning symptom of impending stomatitis and nephritis.

The pathogenesis of the bismuth gum line was investigated soon after the introduction of bismuth in the therapy of syphilis. Similar phenomena were known to occur in cases of occupational lead poisoning and from the use of mercury in the treatment of syphilis. Azoulay,[5] Biberstein,[6] Rothman and Kurz,[7] Löhe and Rosenfeld,[3] Dér,[8] Komayo [9] and many other investigators have made histologic and chemical studies of bismuth impregnation of the gums. The consensus was and still is that the black deposits consist of granules of bismuth sulfide which develop where the soluble bismuth salts, circulating in the blood stream, come in contact with hydrogen sulfide. This gas is formed by bacteria from proteins in decaying organic matter. Tartar and decaying teeth, together with poor dental hygiene, are the most frequent conditions in which a constant development of hydrogen sulfide takes place. There-

3. Löhe, H., and Rosenfeld, H.: Wismutpigmentierungen der Blasenschleimhaut, Dermat. Ztschr. **57**:250, 1929.

4. McCarthy, F. T., and Dexter, S. O., Jr.: Oral Manifestations of Bismuth, New England J. Med. **213**:345, 1935.

5. Azoulay, R.: Stomatite bismuthique, Presse méd. **30**:134, 1922; abstracted, Zentralbl. f. Haut- u. Geschlechtskr. **5**:255, 1922.

6. Biberstein, H.: Ueber die Wismutbehandlung des Syphilis, Deutsche med. Wchnschr. **49**:1518, 1923.

7. (*a*) Rothman, S., and Kurz, R.: Ueber den Chemismus des Wismutsaumes, Klin. Wchnschr. **5**:943, 1926; (*b*) Chemische Untersuchungen ueber Wismutstomatitis, abstracted, Zentralbl. f. Haut- u. Geschlechtskr. **20**:232, 1926.

8. Dér, O.: Entstehung und Histologie des Wismutsaumes, Gyógyászat **66**: 25, 582, 1926; abstracted, Zentralbl. f. Haut- u. Geschlechtskr. **21**:509, 1927.

9. Komayo, G.: Ueber eine histochemische Nachweismethode der Resorption, Verteilung und Ausscheidung des Wismuts in den Organen, Arch. f. Dermat. u. Syph. **149**:277, 1925.

fore, bismuth sulfide is formed in the mouth almost regularly during bismuth medication. But hydrogen sulfide is not only formed in the oral cavity. It is constantly present in the colon. It is here that one should also expect bismuth melanosis. However, there have been sufficient postmortem examinations of bismuth-treated syphilitic patients to show that bismuth melanosis in the colon is extremely rare. Micseh [10] observed 2 cases of black discoloration involving the large intestine from the ileocecal valve to the anus. In these cases the typical granula-

Fig. 1.—Vaginal melanosis. Notice the fine black dots (papillae) on the vulva. The black area in the center of the picture is not shadow but black discoloration of the vaginal mucosa.

tion and reactions due to bismuth sulfide were seen mainly in the capillary endothelial cells of the upper strata of the connective tissue. The condition in these cases was well differentiated from other pigmentations of the colon, e. g. Pick's melanosis. Jadassohn [11] observed

10. Micseh, G.: Wismut-Melanose der Dickdarmschleimhaut, Beitr. z. path. Anat. u. z. allg. Path. **92**:147, 1933.

11. Jadassohn, J., in discussion on Müller, H., and Blass: Demonstration zur Wismutbehandlung, Arch. f. Dermat. u. Syph. **145**:348, 1924.

a case of complete melanosis of the oral mucosa. Löhe and Rosenfeld [3] observed bismuth melanosis of the urinary bladder. Black smegma and black margins in infected tonsils during bismuth treatment are known.

In spite of the fact that decaying organic matter is present in the uterus or vagina under many conditions, melanosis of the vagina seems to be as rare as melanosis of the colon. As far as I know, no cases have been reported as yet. In the many syphilitic patients who were receiving injections of a bismuth preparation and simultaneous vaginal treatment for purulent or ulcerative conditions (gonorrhea, cervicitis), I have never seen melanosis of the vagina. I therefore feel justified in presenting the following cases.

REPORT OF A CASE

Mrs. X. Y., a white woman aged 30, was referred to me for radiation therapy of cancer of the cervix on Jan. 18, 1939. She had been bleeding since about June

Fig. 2.—Bismuth deposits (black lines) in the gums.

1938. A large cauliflower growth had been removed from the cervix in January 1939. From January 18 to February 28 the patient was treated with high voltage roentgen rays in protracted and fractional doses. A total of 6,800 r filtered through 0.5 and 1 mm. of copper at 200 kilovolts, 15 milliamperes and 50 cm. distance was given through five portals. There was a moderate reaction of the skin, which healed with dry scaling. This course was followed by treatment of the cervix with radium from April 4 to April 8. A dose of 3,070 milligram hours was given by means of tubes placed in the cervical crater. The filtration was 1.5 mm. of brass plus 0.3 mm. of platinum. There was a good response. The crater became clean and small. The patient was in excellent general condition and gained much weight.

But in September she started complaining about pain in the back and vaginal discharge. The crater was larger again and had hard, infiltrated edges and a necrotic floor. The vaginal mucosa was normal. A new course, of 3,000 r, high voltage roentgen rays was given from September 9 to September 29. At an examination on this day the vagina appeared black. There was still a large necrotic crater of the cervix, with much foul discharge, but the vaginal mucosa seemed normal except for its color. The condition looked much like a submucosal

hemorrhage, but no cause for such a large extravasation could be discovered. Until November 20 no change in the color of the vagina took place.

The patient had a syphilitic infection of unknown duration. She had Argyll Robertson pupils and a 4 plus Kahn reaction of the blood. She had received a total of 83 cc. of a preparation of basic bismuth salicylate (bismogenol), yielding 4.15 Gm. of bismuth, from Oct. 29, 1938, to Nov. 10, 1939. These injections were given at intervals of approximately five days, in conjunction with liver extract (Dr. Decker). This treatment was well tolerated.

In November 1939 the patient had a black linear deposit of bismuth along the gums and black spots and dots (papillae) on the edges of the tongue corresponding to the interdental spaces. There were many deposits of tartar and decayed and filled teeth.

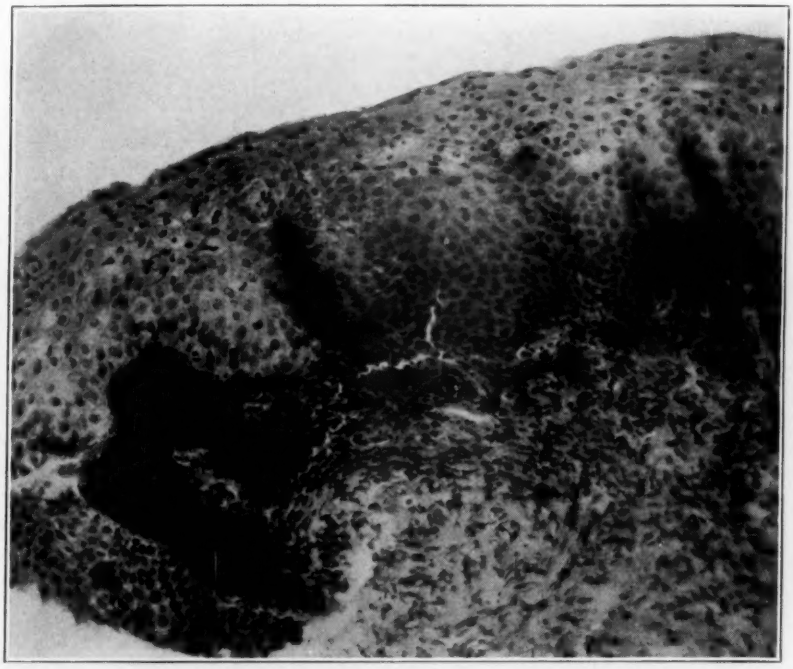

Fig. 3.—Bismuth deposits in the papillae and in the superficial submucous connective tissue (hematoxylin and eosin, low power).

The vaginal mucosa was still almost entirely velvety black. There were only a few small areas of lighter color crossed by black lines, corresponding to the columnae rugarum. There were some areas of slightly black discoloration around the urethral orifice and some fine black points on both sides of the vulva, probably corresponding to papillae.

The rectal mucosa was of normal appearance. A specimen of tissue was taken from the edge of the black area in the posterior vaginal wall and prepared for histologic study in Mount Sinai Hospital.

Histologic Examination.—The vaginal epithelium was normal. The underlying submucosa showed slight increase of cells, mainly lymphocytes. The papillae were mostly slender. Groups of them contained black bodies, apparently the

deposits of bismuth. They consisted of black amorphous granules, which were mainly accumulated within endothelium cells. This is particularly true of cells in some papillae. Some small but black granules were found in intercellular spaces. There was little inflammatory reaction, hardly more than in areas containing none or scarcely any bismuth.

The patient has never been exposed to or given treatment with metal salts, which are liable to produce melanosis, particularly silver and lead. Owing to

Fig. 4.—The deposit in the papillae consists of cell-shaped bodies, which apparently are endothelial cells impregnated with bismuth sulfide (high power).

the history of the orally administered bismuth compound and deposits of the same color, together with the history of long and intensive bismuth therapy, it seemed most likely that the melanosis was caused by bismuth sulfide. To prove this several histochemical reactions were performed.

1. Komayo's reaction (modification of Léger's method). The deparaffinized sections were stained with a mixture of 2 per cent quinine sulfate solution and 4 per cent potassium iodine solution, to which some drops of nitric acid had

been added. After a minute, the sections were quickly washed in weak nitric acid, dehydrated and counterstained with gentian violet. The deposits in the sections showed bright yellow halos. This reaction is supposed to be specific for bismuth deposits.

2. The sections were treated with hydrogen peroxide, which decolorized the black-brown granules almost completely. The color came back after the sections were exposed to freshly developed hydrogen sulfide for five to twenty minutes. Then the deposits appeared black, darker than they had been before.

COMMENT

Bismuth melanosis, the pathogenesis of which is supposed to be "completely plain," [12] still has its problems. Why does it rarely occur in other areas than in the mouth? Why is it seen in the colon so rarely, in spite of the constant formation of hydrogen sulfide there? Which factors cause the unusual impregnation with bismuth sulfide in some cases, while no melanosis is observed in many similar cases?

SUMMARY

The various types of melanosis caused by bismuth medication are reviewed. A case is described in which bismuth melanosis of the entire vagina occurred in a syphilitic patient with an ulcerative cervical cancer.

Technical assistance was given by Dr. N. Enzer, Director of Laboratories of Mount Sinai Hospital, and by his staff, especially Miss A. Leininger and Miss G. Ballard. Mr. L. C. Massopust, Marquette Medical School, made the photomicrographs. Dr. H. G. Decker referred the patient to me and permitted the publication of the case.

12. Juliusberg, F.: Die Nebenwirkungen der Wismutbehandlung, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol. 18, p. 441.

RELAPSING EARLY ACUTE ARSENICAL ERYTHEMA

REPORT OF TWO CASES

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In a recently published article [1] we reported 11 cases of early acute arsenical erythema. In that article we stated that "Not a single recurrence of exactly this type of reaction has ever been reported." Gastrointestinal disturbances and nitritoid crises seemed to be the most common complications when arsphenamine therapy was resumed.

Since then we have observed 2 cases in which the symptoms characterizing early acute arsenical erythema reappeared one or more times with the resumption of injections of arsenic. Fever, eruptions and adenitis and in 1 case conjunctivitis and punctate keratitis occurred after treatment with arsenicals was resumed. The intensity of these reactions decreased with the number of injections, and administration of the drugs was not permanently stopped because of them.

Further search of the literature shows that Milian [2] himself admitted the possibility of a recurrence of the "erythema of the ninth day." He stated that the recurrence takes place chiefly in patients with erythema multiforme eruptions. The behavior in our 2 cases suggests a close relation between this type of eruption and the so-called "toxic eruptions" due to other drugs. Because of the unusual features presented by 1 of our cases a detailed report may be of interest.

REPORT OF CASES

CASE 1.—C. F., a Negress aged 22, was admitted to Bellevue Hospital on Feb. 24, 1939, with a generalized maculopapular rash diagnosed as secondary syphilis. The Wassermann reaction of the blood was strongly positive, although it had been negative six weeks earlier when her husband was found to have secondary syphilis. She was included in a series of patients with early syphilis

From the Department of Dermatology and Syphilology, New York University College of Medicine, and the Department of Dermatology and Syphilology, Third Medical Division (New York University), Bellevue Hospital, service of Dr. Edward R. Maloney.

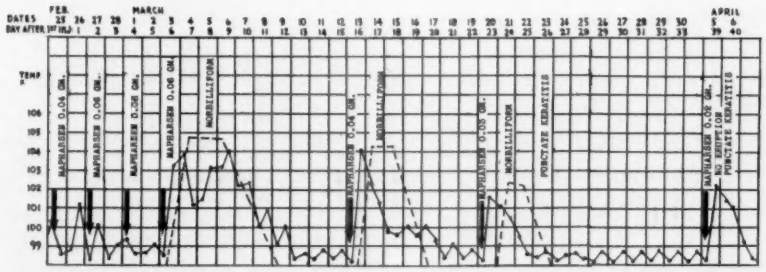
1. Cañizares, O., and Thomas, E. W.: Early Acute Arsenical Erythemas, Arch. Dermat. & Syph. **39**:867-876 (May) 1939.

2. Milian, G.: Les érythèmes interthérapeutiques du neuvième jour, Bull. Acad. de méd., Paris **109**:704-711 (May) 1933.

who were given injections of mapharsen three times a week for the first four weeks of their treatment.

On February 25 she received 0.04 Gm. of mapharsen, without difficulty. On February 27 she received 0.06 Gm. On March 1 and 3 she was again given 0.06 Gm., with no immediate reaction. On the evening of March 3, seven days after the first injection and about twelve hours after the fourth, her temperature rose to 103.8 F. This was preceded by a chill and was associated with nausea and vomiting. She had no sore throat, but the following day a generalized erythema was noted and the conjunctivas of both eyes were injected. She also had some photophobia and increased lacrimation. She had several slightly tender cervical nodes. The fever lasted five days, and the erythema was entirely gone in four days.

No further treatment was attempted until five days after her temperature had become normal. On March 13 she received 0.04 Gm. of mapharsen, which was followed within a few hours by a rise in temperature to 104 F. Nausea and vomiting started about two hours after the injection. On the following morning she again had a generalized erythema, which was entirely macular and consisted of red blotches. Her conjunctivas were injected, and photophobia was present. Her throat was not sore, but she had a "strawberry" tongue, with bright red raised



Temperature chart for C. F., a Negress aged 22. Dotted line indicates intensity and duration of rash.

papillae. Within two days the condition on the tongue and the rash cleared up, but she continued to complain of nausea and generalized aches and pains for another two days.

On March 21 she was given 0.02 Gm. of mapharsen, which was followed by nausea and vomiting and a rise in temperature to 101.4 F. The following day she again had a generalized erythematous blotchy rash. There was less injection of her conjunctivas than on the two previous occasions, but she complained of pain in her eyes and cloudiness of vision. Examination revealed superficial punctate keratitis, confirmed by consultation with the ophthalmic service. The fever and eruption lasted for less than two days, but the keratitis remained for ten days.

On April 5 she was given 0.02 Gm. of mapharsen. Her temperature rose that evening to 102.4 F. No eruption occurred, but she had mild conjunctivitis, associated with punctate keratitis, which lasted for five days.

On April 13 and 22 she was given 0.02 Gm. of mapharsen with 8 minims (0.49 cc.) of epinephrine hydrochloride (1 to 1,000 dilution). She had slight and brief rises in temperature on both occasions but no rash, nausea or vomiting. Her eyes, however, showed slight keratitis for several days after each injection.

On April 25 she was given 0.3 Gm. of acetylglucoarsphenamine intramuscularly, with no reaction. This was followed by eight injections of bismuth subsalicylate

in the outpatient department. Mapharsen was then tried again in doses of 0.01 Gm., without experiencing any difficulty. The dose was increased gradually to 0.06 Gm. She now has a negative Wassermann reaction of the blood and is continuing her treatment without difficulty. The ophthalmic service has reported that both corneas are normal. Treatment with mapharsen was resumed only after all symptoms and the superficial keratitis had subsided. Slit lamp examinations at no time revealed anything resembling interstitial keratitis.

CASE 2.—A Chinese man aged 60 was admitted to Bellevue Hospital with secondary syphilis. He was treated with neoarsphenamine, starting with 0.3 Gm. Seven days after his first injection and one day after the second, fever developed, with a temperature of 103 F. On the following day he had a generalized scarlatiniform rash and a sore throat. Four days after the disappearance of all symptoms he was again given neoarsphenamine, which was followed by another scarlatiniform eruption which lasted only for about twenty-four hours. His temperature rose to 102 F. but became normal within two days. Subsequent injections of the same drug were well tolerated.

THE USE OF SULFANILAMIDE IN DERMATOLOGY

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The introduction of sulfanilamide to the medical profession in 1936 has brought about many changes in therapy in practically every field of medicine. Probably there is no field or specialty in which its value has not been tested clinically as well as experimentally in the laboratory. Nor is there any field in which its value has not been proved as a decided aid to therapy of conditions for which there has been heretofore no valuable remedy.

With the introduction of any new effective drug there is a tendency to extend its use more or less promiscuously. Such spectacular results were obtained with sulfanilamide in many cases of streptococcic infections that it was soon used for all recalcitrant ailments. Its improper use was partly due to the popular belief at the outset that the drug was harmless and did not cause any untoward manifestations. This practice precipitated a large number of untoward and serious reactions, which in turn have caused a wave of skepticism among both patients and physicians. This is unfortunate, because many patients for whom the drug is indicated are denied its benefits owing to a false fear on the part of the physician or of the patient himself.

The purpose of this communication is to present an unbiased evaluation of sulfanilamide in the field of dermatology.

Domagk [1] in 1935 reported favorable therapeutic effects on hemolytic streptococcic infections in mice from the use of a dye (the hydrochloride of 4-sulfamido-2′,4′-diaminoazobenzene) which was called prontosil. Later another substance (disodium 4-sulfamidophenyl-2′-azo-7′-acetylamino-1′-hydroxynaphthalene-3′-6′-disulfonate) was introduced; this was known as prontosil soluble or prontosil S and later as prontosil and as neoprontosil and recently has been given the nonproprietary name azosulfamide. Tréfouël, Tréfouël, Nitti, Nitti and Bovet [2] found that the action of these two preparations was due to a common breakdown

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From the Clinics of Leslie M. Smith, M.D., and Raymond P. Hughes, M.D.
Thesis submitted to the Faculty of the Graduate School of Medicine of the University of Pennsylvania, in partial fulfilment of the requirements for the degree of Master of Medical Science (M. S. [Med.]) for graduate work in dermatology and syphilology.

1. Domagk, G.: Deutsche med. Wchnschr. **61**:250, 1935.

2. Tréfouël, J.; Tréfouël, J. (Mme.); Nitti, J.; Nitti, F., and Bovet, D.: Compt. rend. Soc. de biol. **120**:756, 1935.

product. This substance was paraaminobenzenesulfonamide, to which the name sulfanilamide was applied by the Council on Pharmacy and Chemistry of the American Medical Association.

The exact mode of action of sulfanilamide is not yet understood. According to Keefer,[3] the following suggestions have been offered as to its action: 1. It is a bacteriostatic agent. 2. It stimulates phagocytosis. 3. It neutralizes bacterial toxins. 4. It is bactericidal under certain conditions. 5. It delays growth of organisms until mononuclear phagocytes accumulate. 6. It alters organisms so that phagocytosis can take place. From the work of Bliss and Long [4] and Keefer and Rantz,[5] it is evident that at least in hemolytic streptococcic infections the action of sulfanilamide is bacteriostatic.

Since the early work sulfanilamide has been found of definite value in a number of infections caused by a variety of organisms. Only the conditions related to dermatology are within the scope of this paper.

From the standpoint of convenience and effectiveness sulfanilamide is probably best administered orally in tablet form. Although the drug is soluble in water only to a small degree (0.8 per cent) and is only slightly absorbed in the stomach, the absorption from the small intestine is rapid and definite.[6] In patients who are unable to swallow or who are unable to retain the drug owing to nausea, the injectable form of sulfanilamide is of course preferable. To accelerate absorption when administration of the drug is begun a large volume of water should be given. When the proper concentration of the compound in the blood is reached, however, it is well to restrict the fluid intake in order to help maintain this level. Sulfanilamide is eliminated almost entirely by the kidneys.[7] As yet there is no safe solvent for sulfanilamide except water.

To a large degree the success obtained from the administration of sulfanilamide is dependent on the promptness with which the proper concentration in the tissues and in the blood is reached and the maintenance of this concentration. According to Long, Bliss and Feinstone [7] a blood concentration of from 10 to 15 mg. per hundred cubic centimeters is indicated for severe infections. For mild or moderately severe infections a blood concentration of from 5 to 10 mg. per hundred cubic centimeters is probably sufficient. Keefer [3] stated that from 7 to 10 mg.

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3. Keefer, C. S.: New England J. Med. **219**:562, 1938.

4. Bliss, E. A., and Long, P. H.: Observations on Mode of Action of Sulfanilamide, J. A. M. A. **109**:1524 (Nov. 6) 1937.

5. Keefer, C. S., and Rantz, L. A., cited by Keefer.[3]

6. Marshall, E. K., Jr.; Cutting, W. C., and Emerson, K., Jr.: Toxicity of Sulfanilamide, J. A. M. A. **110**:252 (Jan. 22) 1938.

7. Long, P. H.; Bliss, E. A., and Feinstone, W. H.: Mode of Action, Clinical Use and Toxic Manifestations of Sulfanilamide: Further Observations, J. A. M. A. **112**:115 (Jan. 14) 1939.

per hundred cubic centimeters is adequate for most infections. In order to establish and maintain these levels in the blood and tissue there is some question as to the size of dosage and as to the frequency with which the drug should be given. The time between doses has been shortened greatly during the past few months. At first the drug was given at six and eight hour intervals, whereas now it is most frequently given at four hour intervals. Possibly in the future it will be learned that the interval should be shortened still more in order to keep the blood and tissue fluids supplied with fresh sulfanilamide. Keefer [8] and Long, Bliss and Feinstone [7] began treatment with approximately 60 mg. per kilogram (½ grain per pound) of body weight as the initial dose. They then continued with about 15 to 20 mg. per kilogram (1/10 to 3/25 grain per pound) of body weight at four hour intervals. As the drug is excreted rapidly it is most important to give it at regular four hour intervals, both day and night, in order to maintain an adequate concentration in the blood and in the tissues.

The question as to the duration of the treatment is of considerable importance and has not as yet been definitely settled. When the drug was first introduced it was the idea of many that its administration should not be continued longer than a few days. Most writers now, however, have agreed that the period of administration may safely be lengthened when indicated. Long, Bliss and Feinstone [7] now prefer to give the drug until the patient has practically recovered and with some purulent infections to continue administration for at least ten days after the patient is well. This will assure fewer recurrences.

Most authorities agree that it is not advisable to administer saline cathartics during the course of sulfanilamide therapy. No other drugs seem to be contraindicated. In fact, when other drugs are indicated they should be given along with sulfanilamide. Alcohol should be forbidden, as it has a tendency to accentuate the cerebral symptoms.

Long and Bliss [8] recommended the administration of sodium bicarbonate at all times to combat acidosis. In 1937 Southworth [9] called attention to the fact that patients receiving sulfanilamide had a fall in the carbon dioxide–combining power of the plasma which he interpreted as indicating an acidosis. The investigations of Hartmann, Perley and Barnett,[10] on the other hand, seem to prove that the usual disturbance in the acid-base balance produced by sulfanilamide is actually an alkalosis.

The clinical use of sulfanilamide has resulted in a rather wide variety of toxic manifestations.[7] With the continued use of the product there

8. Long, P. H., and Bliss, E. A.: South. M. J. **30**:479, 1937.

9. Southworth, H.: Proc. Soc. Exper. Biol. & Med. **36**:58, 1937.

10. Hartmann, A. F.; Perley, A. M., and Barnett, H. L.: J. Clin. Investigation **17**:465, 1938.

seems to be a growing list of toxic features which have not been manifest previously. In experimental animals the toxicity is low,[11] but toxic symptoms of some degree are demonstrable in a large number of human beings treated. Fortunately, by far the large majority of these are harmless and are relieved by withdrawal of the drug, and few have been reported which are severe and definitely dangerous.

MILD REACTIONS

Among the acute toxic reactions of a milder nature observed after the administration of sulfanilamide to man are fever, anorexia, cyanosis, nausea, vomiting, dizziness, mental confusion and excitement. These, when they occur, usually come on within a short time after the first dose is given. Although not dangerous, they are often alarming to both patient and physician if they are not aware of the likelihood of their occurrence. Rarely in my experience have such manifestations been severe enough to warrant discontinuance of administration of the drug. Long, Bliss and Feinstone [7] expressed the opinion that when graver complications develop they are preceded soon after the administration of the drug by fever, which is consequently to be regarded as a danger sign. They recommended discontinuance of administration of the drug when an unexplained fever develops. Sulfanilamide fever usually develops between the fifth and the tenth day of treatment.

The mechanism of cyanosis during the administration of sulfanilamide is as yet unexplained. Marshall and Walzl [12] expressed the opinion that the formation of methemoglobin is always responsible for the cyanosis. It is not regarded as a serious complication, however, and does not warrant discontinuance of the treatment.

Most of the other minor symptoms are thought to be of cerebral origin and in the majority of instances will disappear or become much less annoying within twenty-four to forty-eight hours. With ambulatory patients who must attend to active and exacting duties there is occasionally necessity for withdrawal of the drug on this account.

MAJOR COMPLICATIONS

Of the serious or major complications resulting from the use of sulfanilamide, probably the most common is anemia. It occurred in 4 per cent of a series of over 500 patients treated in Johns Hopkins Hospital.[13] Price and Myers [14] reported its occurrence in 5 per cent

11. Bieter, R. N.: Journal-Lancet **59**:139, 1939.

12. Marshall, E. K., Jr., and Walzl, E. M.: Bull. Johns Hopkins Hosp. **61**:140, 1937.

13. Wood, W. B.: Anemia During Sulfanilamide Therapy, J. A. M. A. **111**:1916 (Nov. 19) 1938.

14. Price, A. E., and Myers, G. B.: Treatment of Pneumococcic Pneumonia with Sulfanilamide, J. A. M. A. **112**:1021 (March 18) 1939.

of a series of 115 cases. It usually appears in twenty-four to seventy-two hours after the onset of medication, and the earliest signs are those of jaundice. Wood [15] has reported 1 death from hemolytic anemia. If administration of the drug is discontinued and the proper steps are taken, recovery almost invariably occurs.

Jaundice is a common toxic symptom which necessitates withdrawal of the drug. It is usually hemolytic but occasionally is due to hepatic damage. Cline [16] has reported 1 case of acute yellow atrophy of the liver following administration of sulfanilamide.

Neuritis is an extremely rare toxic manifestation. Bucy [17] reported 1 case of optic neuritis which gradually cleared up after administration of the drug was discontinued.

Agranulocytosis is a rare but probably the most serious of all complications and is usually fatal. Death occurs within two or three days after the onset of the agranulocytosis. Kracke [18] has collected 9 cases which occurred as a result of sulfanilamide therapy. A few others who have reported cases are Ballenger,[19] Culbreath,[20] Johnston,[21] Jones and Miller [22] and Long and Bliss.[23] The condition rarely develops until the patients have taken the drug for two weeks or longer. Myers [24] stated the belief that there is little danger of this complication developing if warning signs, such as fever and dermatitis, are heeded.

CUTANEOUS REACTIONS

Since the first use of sulfanilamide there have been numerous reports of varying types of cutaneous toxic reactions. Long, Bliss and Feinstone [7] reported dermatitis occurring as a complication in 1.6 per cent of his patients, while Hageman and Blake [25] reported its occurrence in as many as 15 per cent of all patients they had treated.

The usual eruption is morbilliform, although several other types have been reported. Among the first to report a toxic cutaneous reaction

15. Wood, H.: South. M. J. **31**:646, 1938.
16. Cline, E. W.: Acute Yellow Atrophy of Liver Following Sulfanilamide Medication, J. A. M. A. **111**:2384 (Dec. 24) 1938.
17. Bucy, P. C.: Toxic Optic Neuritis Resulting from Sulfanilamide, J. A. M. A. **109**:1007 (Sept. 25) 1937.
18. Kracke, R. R.: Relation of Drug Therapy to Neutropenic States, J. A. M. A. **111**:1256 (Oct. 1) 1938.
19. Ballenger, H. C.: Ann. Otol., Rhin. & Laryng. **46**:1129, 1937.
20. Culbreath, P. H.: J. South Carolina M. A. **34**:307, 1938.
21. Johnston, F. D.: Lancet **2**:1044, 1938.
22. Jones, H. W., and Miller, C. P.: J. Lab. & Clin. Med. **24**:121, 1938.
23. Long, P. H., and Bliss, E. A.: Canad. M. A. J. **37**:457, 1938.
24. Myers, G. B.: J. Michigan M. Soc. **38**:302, 1939.
25. Hageman, P. D., and Blake, F. G.: Specific Febrile Reaction to Sulfanilamide: Drug Fever, J. A. M. A. **109**:642 (Aug. 28) 1937.

to the drug were Newman and Sharlit,[26] who reported 4 cases of eruptions in areas exposed to sunlight. They were able to reproduce the same type of reaction on other surfaces by exposure to ultraviolet irradiation. Menville and Archinard [27] reported a series of 4 cases of reactions also on exposed surfaces after administration of the drug. Frank [28] reported 2 cases in which the eruption was more pronounced on the surfaces exposed to sunlight, but lesions of erythema multiforme were also present on covered surfaces of the body. Goodman and Levy [29] reported 2 cases of a maculopapular generalized eruption occurring after small doses of sulfanilamide were taken, in 1 of which a scratch test with the drug gave a positive reaction. Salvin [30] reported a case of dermatitis due to sulfanilamide in which there was a positive reaction to patch tests and in which a small dose caused a recurrence of the dermatitis. Schwentker and Gelman [31] in a series of 180 cases reported a morbilliform eruption in 6 per cent of cases, in which fever and malaise always accompanied the eruption. The eruption was usually generalized. Finney [32] reported a case of severe itching and edema of the face, arms and chest accompanied by a generalized maculopapular eruption. There was moderate elevation of temperature. Schlesinger and Mitchell [33] studied 10 cases of sulfanilamide dermatitis and noted the syndrome of prodromal fever and a morbilliform eruption occurring most commonly on the ninth day in all cases and splenomegaly in many. Feldman [34] and DeOreo [35] both reported cases in which scarlatiniform eruptions developed on the covered surfaces of the body after three weeks' treatment (Feldman) and after two days' administration of the

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26. Newman, B. A., and Sharlit, H.: Sulfanilamide: Photosensitizing Agent of Skin, J. A. M. A. **109**:1036 (Sept. 25) 1937.

27. Menville, J. G., and Archinard, J. J.: Skin Eruptions in Patients Receiving Sulfanilamide: Report of Four Cases, J. A. M. A. **109**:1009 (Sept. 25) 1937.

28. Frank, L. J.: Dermatitis from Sulfanilamide, J. A. M. A. **109**:1011 (Sept. 25) 1937.

29. Goodman, M. H., and Levy, C. S.: Development of Cutaneous Eruption (Toxicodermatosis) During Administration of Sulfanilamide: Report of Two Cases, J. A. M. A. **109**:1009 (Sept. 25) 1937.

30. Salvin, M.: Hypersensitivity to Sulfanilamide, J. A. M. A. **109**:1038 (Sept. 25) 1937.

31. Schwentker, F. F., and Gelman, S.: Bull. Johns Hopkins Hosp. **61**: 136, 1937.

32. Finney, J. O.: Severe Dermatitis Medicamentosa Following Administration of Sulfanilamide, J. A. M. A. **109**:1982 (Dec. 11) 1937.

33. Schlesinger, E. R., and Mitchell, W. L., Jr.: Sulfanilamide Eruption: Study of Patients with Morbilliform Rash and of Their Subsequent Reactions, Am. J. Dis. Child. **56**:1256 (Dec.) 1938.

34. Feldman, S.: Pemphigus Treated with Sulfanilamide: Sulfanilamide Eruption, Arch. Dermat. & Syph. **39**:601 (March) 1939.

35. DeOreo, G. A.: Dermatitis Medicamentosa from Sulfanilamide, Arch. Dermat. & Syph. **40**:332 (Aug.) 1939.

drug (DeOreo). Loveman and Simon [36] reported a case of fixed eruption accompanied by stomatitis following ingestion of the drug. The symptoms subsided on withdrawal of the drug and were reproduced when it was given again. Patch tests gave negative results on unaffected areas but positive results on previously affected skin. Noun [37] also reported a case with lesions of the mucous membranes accompanying an urticarial type of eruption. Schonberg [38] reported a case in which a purpuric eruption developed after four days' treatment with the drug. A few weeks later the patient was given 5 grains (0.32 Gm.) of sulfanilamide and a generalized scarlatiniform eruption and high fever developed. Cleveland [39] reported a case of varioliform eruption following the use of sulfanilamide. The eruption was not confined to the exposed surfaces, and some of the lesions resembled erythema multiforme. There was no itching, and the pustules did not produce any scarring. Costello [40] presented a case in which lupus erythematosus developed for the first time about three months after the patient had been given sulfanilamide for a vaginal infection. The eruption appeared over exposed areas after severe sunburn. Bettley and Simon [41] reported a case of bullous eruption occurring after the administration of sulfanilamide. The patient first presented a morbilliform rash accompanied by malaise, nausea and vomiting. Administration of the drug was continued, and several days later a bullous type of eruption appeared on the exposed surfaces after exposure to sunlight. Myers, Vonder Heide and Balcerski [42] reported on exfoliative dermatitis in a patient who had taken sulfanilamide for twenty-eight days. It was accompanied by purpura, fever and transient jaundice. The condition had started with a morbilliform eruption. A positive reaction to a patch test caused a flare-up in the dermatitis.

To summarize, the following types of cutaneous reactions have been reported in the literature: morbilliform eruption, dermatitis from photosensitization, erythema multiforme, scarlatiniform eruption, fixed eruption, stomatitis, urticaria, purpura, varioliform eruption, and exfoliative dermatitis.

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36. Loveman, A. B., and Simon, F. A.: Fixed Eruption and Stomatitis Due to Sulfanilamide, Arch. Dermat. & Syph. **40**:29 (July) 1939.

37. Noun, M. H.: Erosions of Oral Mucosa and Urticaria of Body Following Small Doses of Sulfanilamide, Arch. Dermat. & Syph. **37**:1045 (June) 1938.

38. Schonberg, I. L.: Purpuric and Scarlatiniform Eruption Following Sulfanilamide, J. A. M. A. **109**:1035 (Sept. 25) 1937.

39. Cleveland, D. E. H.: Varioliform Eruption from Sulfanilamide, Arch. Dermat. & Syph. **39**:693 (April) 1939.

40. Costello, M.: Lupus Erythematosus Precipitated by Sunlight After Sulfanilamide Therapy, Arch. Dermat. & Syph. **39**:598 (March) 1939.

41. Bettley, F. R., and Simon, P.: Brit. M. J. **1**:1177, 1939.

42. Myers, G. B.; Vonder Heide, E. C., and Balcerski, M.: Exfoliative Dermatitis Following Sulfanilamide, J. A. M. A. **109**:1983 (Dec. 11) 1937.

In my own experience I have observed 6 cases of generalized maculopapular or morbilliform eruption, 4 cases of erythema multiforme, 2 of urticaria, 3 cases of a papular dermatitis of the face, neck, forearms and hands following exposure to sunlight, 1 of scarlatiniform eruption and 1 of exfoliative dermatitis. All of these eruptions disappeared promptly on discontinuance of administration of the drug with the exception of the exfoliative dermatitis. This condition was generalized and severe and has been present for several months, without any tendency to disappear in spite of thorough treatment by several competent dermatologists in different parts of the country.

SULFANILAMIDE FOR DERMATOLOGIC CONDITIONS; REVIEW OF THE LITERATURE

Sulfanilamide has been used in the treatment of a large number of dermatologic conditions, with varying degrees of success. As yet there is considerable difference of opinion concerning its value against most cutaneous diseases, but this is natural in view of the fact that it is still a new drug and time has not permitted sufficient trial or sufficient observation after its use for a unanimity of opinion to be established. Realization of its proper value will come only as a result of several years' experience and with the exchange of ideas over different parts of the country.

Probably one of the most common uses of sulfanilamide in the field of dermatology is that of the treatment of lupus erythematosus. Ingels [43] reported 5 cases. All 5 patients were greatly improved, and 2 were apparently completely cured. Sulzberger [44] reported on 3 patients with the subacute discoid type of lupus erythematosus. All were greatly improved by the treatment. Other treatment tried previously in the same cases had failed. Abramowitz [45] reported the cure of 3 patients with acute disseminate lupus erythematosus. He stated that he had never before seen this condition cured by other methods of therapy. Belote [46] described 2 patients who had been desperately ill with acute lupus erythematosus but who were at the time of his report in a state of remission after treatment with sulfanilamide. Anderson [47] reported

43. Ingels, A. E.: Lupus Erythematosus Treated with Sulfanilamide, Arch. Dermat. & Syph. **37**:879 (May) 1938.

44. Sulzberger, M. B.: Lupus Erythematosus Treated with Sulfanilamide, Arch. Dermat. & Syph. **39**:610 (March) 1939.

45. Abramowitz, E. W., in discussion on Wise, F.: Discoid Lupus Erythematosus Undergoing Dissemination, Arch. Dermat. & Syph. **38**:661 (Oct.) 1938.

46. Belote, G. H.: Lupus Erythematosus Disseminatus, Arch. Dermat. & Syph. **39**:793 (May) 1939.

47. Anderson, H. F.: Fulminating Acute Lupus Erythematosus Cured by Sulfanilamide, Arch. Dermat. & Syph. **38**:621 (Oct.) 1939.

on a patient with fulminating acute lupus erythematosus who had remained cured for six months after sulfanilamide had been given. The condition was precipitated by the administration of gold sodium thiosulfate. Lindsay [48] reported a case of acute lupus erythematosus in which the eruption had been aggravated by gold therapy. The patient improved greatly from sulfanilamide treatment until a dermatitis developed from the sulfanilamide, at which time its administration was discontinued. She remained free of eruption for two months and then had a recurrence. Sulfanilamide was given again, after which the condition cleared completely, without ill effects from the drug. Wollenberg [49] reported a case of acute disseminated lupus erythematosus which had been extremely resistant to treatment of all types. After the administration of sulfanilamide the condition cleared promptly. Wilson,[50] on the other hand, had a patient with typical acute disseminated lupus erythematosus from the lesions of which a streptococcus was cultured. After well controlled treatment for twelve days the patient failed to show any improvement and died. Jamieson [51] also reported a case of lupus erythematosus disseminatus of four years' duration which showed no response to sulfanilamide and likewise failed to improve with other types of treatment.

Bregman [52] observed a case of erythema multiforme in which sulfanilamide had a definite curative effect. Benefit was noted after twenty-four hours.

Eller [53] treated a patient with pemphigus with sulfanilamide and obtained moderate relief. Caro [54] reported great improvement in 2 cases of pemphigus. Lain and Lamb [55] obtained a spectacular cure of a "pemphigoid" eruption. There had been no recurrence at the time of the report, four weeks later.

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48. Lindsay, H. C. L.: Lupus Erythematosus, Arch. Dermat. & Syph. **39**: 888 (May) 1939.

49. Wollenberg, R. A. C.: Lupus Erythematosus Disseminatus, Arch. Dermat. & Syph. **38**:295 (Aug.) 1938.

50. Wilson, J. F.: Sulfanilamide in Treatment of Acute Lupus Erythematosus, Arch. Dermat. & Syph. **40**:241 (Aug.) 1939.

51. Jamieson, R. C.: Lupus Erythematosus Disseminatus, Arch. Dermat. & Syph. **40**:301 (Aug.) 1939.

52. Bregman, A.: Treatment of Erythema Multiforme Exsudativum with Sulfanilamide: Report of Case, Arch. Dermat. & Syph. **38**:623 (Oct.) 1938.

53. Eller, J. J.: A Case for Diagnosis (Pemphigus? Dermatitis Herpetiformis?), Arch. Dermat. & Syph. **37**:669 (April) 1938.

54. Caro, M. R.: Pemphigus: Treatment with Sulfanilamide; Preliminary Report, Arch. Dermat. & Syph. **37**:196 (Feb.) 1938.

55. Lain, E. S., and Lamb, J. H.: Treatment of Pemphigoid Eruption with Sulfanilamide: Report of Case, Arch. Dermat. & Syph. **37**:840 (May) 1938.

A case of severe generalized impetigo herpetiformis in a pregnant woman was reported by Frank [56] in which complete resolution occurred after sulfanilamide therapy. Improvement was noted on the third day after beginning treatment.

Several cases of various pyogenic dermatoses have been reported in which the condition was improved or cured by sulfanilamide. Abramowitz [57] reported apparent cure in a case of sycosis vulgaris with moderate doses. The response was prompt. Strickler and Stone [58] treated 4 patients with resistant sycosis vulgaris who responded within three weeks to sulfanilamide. The same authors reported 2 cases of impetigo neonatorum and 6 cases of secondary pyogenic dermatoses, in all of which the condition responded to this treatment. In the latter group of cases prolonged treatment was necessary.

Anderson and Halloran [59] failed to obtain any improvement from sulfanilamide in a case of pyoderma gangraenosum.

Mercer [60] successfully treated recurrent lymphangitis (elephantiasis nostras) of the lip which had resisted other forms of treatment.

Wright and Friedman [61] obtained decided improvement of a chronic streptococcic ulcer of the leg with sulfanilamide. These authors also used this drug in a case of infectious eczematoid dermatitis in which Staphylococcus aureus haemolyticus and Streptococcus haemolyticus were found. Complete healing took place in one week.

Thirty-one patients with erysipelas were treated by Iga and Kato [62] with small doses of sulfanilamide. All but 1 showed rapid and complete cure. One patient died, and 3 had recurrences which cleared up rapidly when treatment was resumed. Sulzberger [63] has reported a case of recurrent erysipelas of the forehead and face which was successfully treated with sulfanilamide.

Sandler [64] observed complete disappearance of all symptoms of syphilitic interstitial keratitis within ninety-six hours after sulfanilamide therapy had been instituted.

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56. Frank, L. J.: Impetigo Herpetiformis: Report of Successful Treatment with Sulfanilamide, Arch. Dermat. & Syph. **40**:253 (Aug.) 1939.

57. Abramowitz, E. W.: Sycosis Vulgaris, Improved by Sulfanilamide, Arch. Dermat. & Syph. **37**:1086 (June) 1938.

58. Strickler, A., and Stone, M. J.: Sulfanilamide in Treatment of Pyogenic Dermatoses, Arch. Dermat. & Syph. **40**:244 (Aug.) 1939.

59. Anderson, C. R., and Halloran, D. R.: Pyoderma Gangraenosum, Arch. Dermat. & Syph. **39**:361 (Feb.) 1939.

60. Mercer, S. R.: Recurrent Lymphangitis Treated with Sulfanilamide, Arch. Dermat. & Syph. **39**:1042 (June) 1939.

61. Wright, C. S., and Friedman, R.: Chronic Streptococcic Ulcer of the Skin Responding to Sulfanilamide, Arch. Dermat. & Syph. **39**:554 (March) 1939.

62. Iga, Y., and Kato, T.: Acta dermat. **30**:112, 1937.

63. Sulzberger, M. B.: Recurrent Erysipelas Successfully Treated with Sulfanilamide, Arch. Dermat. & Syph. **40**:498 (Sept.) 1939.

64. Sandler, I. L.: Sulfanilamide Treatment of Syphilitic Interstitial Keratitis, Arch. Dermat. & Syph. **39**:528 (March) 1939.

In the treatment of lymphogranuloma venereum sulfanilamide has apparently been consistently beneficial. Shaffer and Arnold [65] treated 46 patients, in all of whom there was definite improvement. Of 22 patients on whom continued observation was possible, 4 were completely cured, 11 were decidedly improved and 4 failed to return; there were 3 failures. Montel and Nguyen-van-Tho [66] reported 3 cases in which complete recovery occurred. Warren [67] reported approximately 20 per cent improvement from sulfanilamide in a case in which the condition had resisted all treatment for three years. Greenbaum [68] obtained definite improvement in 3 cases in which the eruption had been unaffected by other treatment.

The reports on the treatment of chancroid with sulfanilamide have been almost universally favorable. Kornblith, Jacoby and Wishengrad [69] reported 45 cases of proved chancroid in which cure was obtained without failure by the end of the second week. Eighty grains (5.2 Gm.) of sulfanilamide was given daily for five days and then 40 grains (2.6 Gm.) daily for nine days. Fox [70] treated a patient with an extensive chancroidal ulcer of the penis and obtained complete cure in twenty-eight days. He also reported a case in which a total of 52 Gm. of sulfanilamide was administered without apparent improvement. Lepinay [71] stated that the use of sulfanilamide as a dusting powder was extremely effective against chancroid. For early lesions he used the drug only locally, but for conditions in the late stages he gave the drug both locally and internally. Healing in his cases was rapid, the time necessary for cure being generally one week or less. In 2 cases reported by Schwartz [72] cure of the ulcer and of the ruptured bubos was obtained within two weeks. Chargin [73] reported cure within two weeks of a long-standing chancroidal infection. Rostenberg [74] obtained

65. Shaffer, L. W., and Arnold, E.: Lymphogranuloma Venereum; Especially Its Treatment with Sulfanilamide, Arch. Dermat. & Syph. **38**:705 (Nov.) 1938.

66. Montel, L. R., and Nguyen-van-Tho: Bull. Soc. franç. de dermat. et syph. **45**:652, 1938.

67. Warren, L. H.: Lymphogranuloma Venereum, Arch. Dermat. & Syph. **38**:262 (Aug.) 1938.

68. Greenbaum, S. S., in discussion on Warren.[67]

69. Kornblith, B. A.; Jacoby, A., and Wishengrad, M.: Treatment of Chancroid with Sulfanilamide, J. A. M. A. **111**:523 (Aug. 6) 1938.

70. Fox, H.: Chancroidal Ulcer of Long Standing Cured by Sulfanilamide, Arch. Dermat. & Syph. **38**:660 (Oct.) 1938.

71. Lepinay: Bull. Soc. franç. de dermat. et syph. **45**:1728, 1938.

72. Schwartz, W. F.: Chancroid with Ruptured Bubo Treated with Sulfanilamide, Arch. Dermat. & Syph. **40**:331 (Aug.) 1939.

73. Chargin, L.: Chancroid, Cured with Sulfanilamide: Lymphogranuloma Venereum; Syphilis, Arch. Dermat. & Syph. **38**:476 (Sept.) 1938.

74. Rostenberg, A.: Chancroids Cured with Sulfanilamide, Arch. Dermat. & Syph. **38**:509 (Sept.) 1938.

cure within two weeks in a case of chancroid in which other methods had been used for four months.

PERSONAL EXPERIENCE WITH SULFANILAMIDE

Of 19 patients with erysipelas treated with sulfanilamide, 16 were either rapidly cured or greatly improved and disappeared from observation. Three patients died within twenty-four hours after treatment was instituted; 1 was a man aged 93, and the conditions in the other 2 were severe and unusually extensive when treatment with sulfanilamide was begun. In general this experience coincides with that reported in the literature.

Of 9 patients with erythema multiforme treated with sulfanilamide, in 1 the condition occurred as a dermatophytid associated with an acute dermatophytosis of the feet; the injection of trichophytin intracutaneously produced an iris type lesion similar to those of the disease. There was no improvement from the sulfanilamide. All the other patients responded in from two to five days, and in all remarkable improvement was noted within twenty-four hours. In a patient who was somewhat intolerant to the drug there was a recurrence of the condition, but it disappeared permanently after further administration of the drug.

Three patients with impetigo contagiosa were cured in five, five and nine days, respectively, without the use of local germicidal preparations.

Although a majority of the reports indicate decided benefit from sulfanilamide therapy in patients with lupus erythematosus, my experience has not been so favorable. Only 1 patient was cured by it. Of 5 with discoid conditions, 2 were slightly improved and the others were apparently unaffected. Four patients with acute disseminated lupus erythematosus were benefited to varying extents, but only 1 was cured; this patient, however, was healed in about ten days. One patient obtained moderate improvement for a time and then died after abortion and lobar pneumonia. Sulfanilamide is by no means consistently beneficial in the treatment of lupus erythematosus. Some patients are greatly benefited, and others are uninfluenced by the drug.

Four patients with chronic lymphangitis of streptococcic origin were treated. One of these had been having periodic exacerbations with chills and fever every month or six weeks. After three weeks of sulfanilamide therapy he was well and has had no recurrence for the past year. Two other patients were cured, and 1 was considerably benefited.

A woman with streptococcic stomatitis and cheilitis was definitely improved after twenty-four hours of sulfanilamide treatment. She then disappeared from observation, but I learned later that the condition had cleared up rapidly.

Of 2 patients with typical pemphigus treated with sulfanilamide, neither was apparently influenced.

A patient with an acute bullous eruption which closely resembled pemphigus but with a negative Nikolsky sign showed rapid improvement and was cured in approximately three days. This condition probably belongs to the erythema multiforme group.

A patient with dermatitis herpetiformis received no benefit from sulfanilamide given over two weeks.

Two patients treated for chancroid showed definite and prompt improvement. One disappeared from observation after the first few days of treatment, and further observation was not possible. The other experienced such an unfavorable reaction to the drug that its administration was discontinued at the end of the fourth day, at which time there was about 50 per cent diminution in the size of the ulcer.

A patient with lymphogranuloma venereum was treated with sulfanilamide. The condition was a recurrence of an old infection which had been inactive for approximately four years. After ten days' treatment there was definite improvement, and the patient was not seen again.

A patient with moderately severe herpes zoster accompanied by considerable pain was treated for three days with sulfanilamide. There was no change in the physical signs or in the intensity of the pain.

A patient with recurring furunculosis was treated for one week, without showing evidence of any improvement.

SUMMARY

The history of sulfanilamide therapy is presented, together with its mode of action and toxic manifestations. A review of the literature concerning the treatment of dermatologic conditions and a discussion of my experience are given for the purpose of evaluating sulfanilamide therapy in dermatology.

Apparently the drug is of definite value in the majority of cases of the following conditions: erysipelas, erythema multiforme, impetigo contagiosa, acute disseminate lupus erythematosus, chancroid and streptococcic lymphangitis.

Sulfanilamide appears to be of value in some cases of the following diseases and worthy of further testing: chronic lupus erythematosus, lymphogranuloma venereum, sycosis vulgaris and pemphigus.

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IODOBISMITOL WITH SALIGENIN IN THE TREATMENT OF NEUROSYPHILIS

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After many years of experimental search for a preparation which would produce a significant concentration of bismuth in the central nervous system, Hanzlik, Mehrtens, Gurchot and Johnson [1] introduced iodobismitol (sodium iodobismuthite dissolved in ethylene glycol containing 12 per cent sodium iodide) in 1930. The administration of this preparation to animals resulted in greater amounts of bismuth in the nervous system than were obtained with other available compounds. These findings suggested that iodobismitol might be of exceptional value in the treatment of neurosyphilis, and this theoretic effectiveness was supported by the preliminary clinical studies of Mehrtens and Pouppirt.[2] No further clinical evaluation of this preparation in the treatment of neurosyphilis has been made, although Johnson and Barnett [3] have shown that its use in the routine treatment of early syphilis does not prevent involvement of the nervous system.

Thorough investigation in the laboratory is essential before any drug may be used clinically, but no matter how complete this investigation, it can only suggest the possible therapeutic value. The final evaluation must depend on extensive clinical trial. In cases of neurosyphilis the problem is particularly difficult, because improvement with treatment is at best slow and uncertain. Moreover, comparable controls are not available, since it is not feasible to allow patients to go untreated because of the gravity of neurosyphilis.

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1. Hanzlik, P. J.; Mehrtens, H. G.; Gurchot, C., and Johnson, C. C.: Iodobismitol, a Soluble Bismuth Product for Use in the Treatment of Syphilis: Preliminary Report, J. A. M. A. **98**:537 (Feb. 13) 1932.

2. Mehrtens, H. G., and Pouppirt, P. S.: Iodobismitol in the Treatment for Neurosyphilis, Arch. Neurol. & Psychiat. **26**:1220 (Dec.) 1931.

3. Johnson, G. S., and Barnett, C. W.: The Effect of Iodobismitol upon Spinal Fluid Findings in Early Syphilis, Am. J. Syph., Gonor. & Ven. Dis. **20**:651 (Nov.) 1936.

The results obtained with iodobismitol with saligenin N. N. R. (a solution of sodium iodobismuthite and sodium iodide in propylene glycol containing saligenin and a small amount of acetic acid) in the treatment of syphilis have been previously reported,[4] but no detailed consideration was given to neurosyphilis. The present study is concerned with the effect of treatment in 203 patients with various types of syphilis of the central nervous system. All had received iodobismitol with saligenin and had been under observation for at least six months, and patients who had been given either intraspinal or fever therapy were excluded.

Of the 203 patients, 129 were male, and 74, female. The ages ranged from 13 to 66, with an average of 44 for the males and 39 for the females. The initial diagnosis was tabes dorsalis in 68 patients, dementia paralytica in 44, dementia paralytica with tabes dorsalis in 18, meningovascular neurosyphilis in 22 and asymptomatic neurosyphilis in 51.

Prior to treatment detailed histories were taken, and complete physical and neurologic examinations were made, and these were repeated at approximately six month intervals. At least two examinations of the cerebrospinal fluid were made in all but 12 patients, the total number of examinations being seven hundred and three, or an average of three and a half per patient. The duration of treatment averaged thirty-three months, and the total period of observation, thirty-five months. Many patients were still under treatment at the time this study was terminated.

The method of classification of abnormalities of the spinal fluid was that used by the Cooperative Clinical Group. Group II fluids have a normal or increased cell count, protein content and colloidal gold curve and a positive Wassermann reaction. Group III consists of fluids of the dementia paralytica type. There were no fluids initially in group I. Quantitative Wassermann reactions were used in the evaluation of results, and whenever there was a decrease in titer under treatment, the fluid was considered to be improved. A decided fall in cell count or in protein content, as measured by qualitative globulin tests and the colloidal gold curve, was also classified as improvement, even though in some instances the Wassermann titer did not change. When only minor changes occurred in any of the reactions, the fluid was considered unchanged; but if any increase in the degree of positivity was noted, the condition was regarded as worse. All fluids that became normal were classified as showing reversal of reaction rather than as improved.

The clinical results have been evaluated according to the following terms: (1) much improved, if the symptoms practically disappeared and the progress of the disease was arrested; (2) moderately improved,

4. Barnett, C. W., and Kulchar, G. V.: Iodobismitol in the Treatment of Syphilis, J. A. M. A. **109**:1715 (Nov. 20) 1937.

when the symptoms became less severe; (3) unchanged, if symptoms and signs were not significantly altered, and (4) worse, if there was definite progression. Because of the relatively small number of cases it was found inadvisable to consider separate diagnoses. Consequently the series was left undivided in the final compilation of the data.

Although all patients received iodobismitol with saligenin, many also had other forms of chemotherapy. In this report the therapy was of three types: (1) iodobismitol with saligenin exclusively in intramuscular doses of 2 or 3 cc. one to three times weekly, (2) neoarsphenamine in addition to iodobismitol with saligenin (there was a considerable variation in the amount of neoarsphenamine used, but no patients who received less than a total of 5 Gm. were included) and (3) tryparsamide with or without neoarsphenamine in addition to iodobismitol with

TABLE 1.—*The Results of Treatment with Iodobismitol with Saligenin for One Year in Patients with Neurosyphilis, Compared with Those Obtained by Mehrtens and Pouppirt* [2]

	Mehrtens and Pouppirt, Per Cent	Present Series, Per Cent
Cerebrospinal fluid response		
Reversed	7	10
Improved	42	45
Unimproved	51	45
Clinical response		
Improved	64	61
Unimproved	36	39
Wassermann response		
Reversed	15	25
Improved	25	37
Unimproved	60	38

saligenin (there was again a variation in the amount of tryparsamide, but patients who had less than 30 Gm. were excluded).

Iodobismitol with saligenin has been used in this clinic almost to the exclusion of other heavy metal preparations during the last ten years. We are consequently unable to compare its effectiveness with that of other bismuth preparations used under similar conditions. The evaluation must, therefore, be based on the relative effects of varying amounts of iodobismitol with saligenin, both with and without other forms of chemotherapy. We have accordingly tabulated the data to determine the serologic and clinical results of the three types of therapy outlined above.

In the initial report of Mehrtens and Pouppirt the clinical and serologic results of treatment with iodobismitol alone for one year are given. In the present series there is a similar group of 54 patients who received iodobismitol with saligenin exclusively for one year. A comparison of the results of this form of treatment in these two groups of patients is made in table 1.

The results in the two groups are strikingly similar and suggest that the bismuth compound has a definite therapeutic effect in cases of neurosyphilis. Both the clinical and the serologic results appear exceptionally good for this period of time. This might be interpreted as evidence of a high degree of therapeutic efficacy, but it must be kept in mind that both series comprised ambulatory patients among whom there was a low incidence of advanced neurosyphilis. In cases of this type a rapid response is much more common than in the more advanced stages. If the excellent results are due to the effectiveness of iodobismitol, one might expect that the degree of improvement would vary according to

TABLE 2.—*Comparison of Serologic and Clinical Results in Patients Receiving Less Than and More Than 12 Gm. of Iodobismitol with Saligenin in One Year*

Total Dose of Iodobismitol with Saligenin	Cerebrospinal Fluid Response		Clinical Response	
	Number of Patients	Per Cent Improved	Number of Patients	Per Cent Improved
More than 12 Gm.....	23	57	19	63
Less than 12 Gm.....	26	54	20	60

TABLE 3.—*Comparison of Cerebrospinal Fluid and Clinical Response in Patients Treated for Various Periods with Iodobismitol with Saligenin Exclusively*

Duration of Treatment	Cerebrospinal Fluid Response		Clinical Response	
	Number of Patients	Per Cent Improved	Number of Patients	Per Cent Improved
Six months	18	50	16	63
One year	49	55	41	61
Two years	25	64	21	62

the amount of iodobismitol administered. To test this assumption the patients treated with iodobismitol with saligenin alone for one year have been divided into two approximately equal groups according to the amount received. The clinical and serologic results in patients receiving more than 12 Gm. (approximately one hundred injections) during one year are compared with those in patients receiving less than 12 Gm. in table 2.

From the data in table 2 it appears that there is no correlation between the response and the amount of iodobismitol with saligenin received during one year. However, many of the patients, even though included in the second group, received large amounts of iodobismitol with saligenin. All attempts to segregate groups receiving small amounts of the bismuth preparation led to the inclusion of patients who had great irregularity of treatment, when the period of observation was kept at one year. We have accordingly compared the results obtained

in patients treated with iodobismitol with saligenin alone for periods of six months, one year and two years. The results are shown in table 3.

From table 3 it is evident that the improvement is not proportional to the amount of iodobismitol with saligenin received. Although there is a slight increase in the number of cerebrospinal fluids improved, there is no relation between duration of treatment and the clinical results. The improvement after six months of treatment is greater than can be expected from the natural involution of the disease. It appears that iodobismitol with saligenin has definite therapeutic value, but the maximum effect is achieved during the first few months of treatment.

In order to compare the effect of iodobismitol with saligenin alone with that of iodobismitol with saligenin plus other forms of chemo-

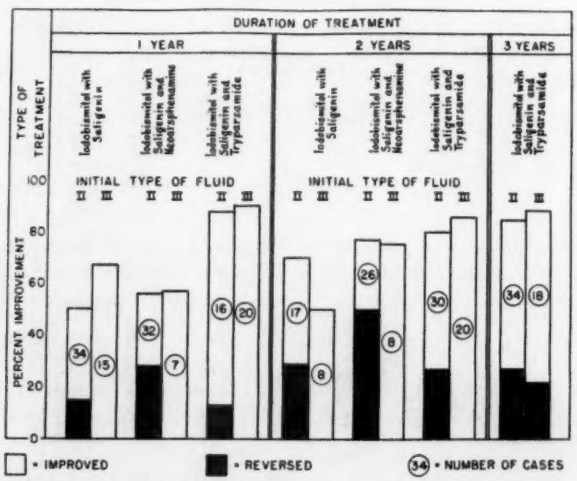

Fig. 1.—Cerebrospinal fluid response to iodobismitol with saligenin alone and in combination with neoarsphenamine or tryparsamide.

therapy, the results of treatment were evaluated at periods of approximately one year and two years. The serologic results, based on the initial type of spinal fluid, are shown in figure 1.

At the end of the first year about one half of the type II spinal fluids were improved with treatment with iodobismitol with saligenin alone. When neoarsphenamine was combined with iodobismitol with saligenin, the percentage of improvement was slightly greater and that of reversal of reaction almost doubled. With the addition of tryparsamide therapy, the incidence of serologic improvement was greatly increased. The percentage of reversal was, however, less than that obtained with other forms of treatment. This probably is due to the fact that tryparsamide therapy was often reserved for patients whose cerebrospinal fluids were refractory to other forms of treatment. In

none of the type III fluids was the reaction reversed, but the greatest improvement occurred in patients who received tryparsamide. Although the patients receiving neoarsphenamine showed a slightly lower incidence of improvement, the number is too small to be of significance.

At the end of the second year the serologic results were similar to those obtained during the first year. The percentage of improvement was generally increased, and the proportion of reversals of reaction was considerably greater. As seen in the results of the first year, the addition of either neoarsphenamine or tryparsamide to iodobismitol with saligenin improved the results. While the total incidence of improvement with tryparsamide at the end of two years is not greater, there is a definite increase in the percentage of reversals of reaction. None

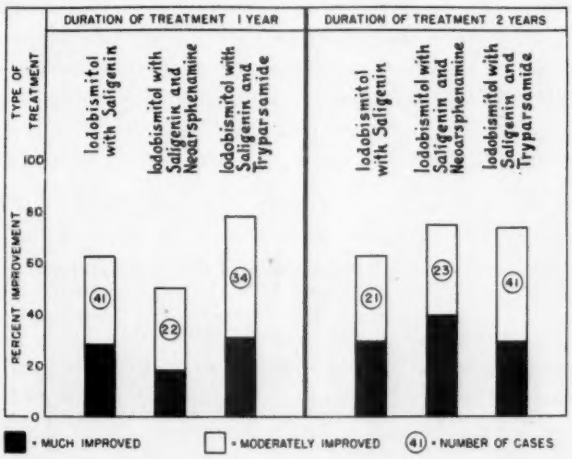

Fig. 2.—Clinical results of treatment with iodobismitol with saligenin alone and in combination with neoarsphenamine or tryparsamide (results in patients with asymptomatic neurosyphilis are not included).

of the type III spinal fluids showed a reversal of reaction during either the first or second years with any of the three methods of treatment. The results of tryparsamide therapy at the end of the third year are included in figure 1, showing an increase in the degree of improvement, despite the fact that there is no change in the percentage of the fluids improved. Data are not available for the results of either iodobismitol with saligenin alone or in combination with neoarsphenamine for the three year period, as practically all patients treated for more than two years received tryparsamide.

The clinical improvement obtained with the three types of therapy at the end of one year and two years is shown in figure 2.

There is striking similarity between figures 1 and 2, indicating that in general clinical and serologic improvement parallel each other. In the unimproved group a few patients are included who became clinically worse during treatment, but these were too scattered to be of significance and have been disregarded. After one year the percentage of clinical improvement with iodobismitol with saligenin alone is greater than that secured with the addition of neoarsphenamine but considerably less than that obtained with the addition of tryparsamide. At the end of two years, however, the improvement secured with iodobismitol with saligenin and either neoarsphenamine or tryparsamide is greater than with the bismuth compound alone. When iodobismitol with saligenin is used alone or in combination with tryparsamide, the clinical improvement, both in amount and in degree, is practically the same after one year and after two years of treatment. This indicates that when improvement occurs with these two types of therapy, it does so promptly and is then sustained. With the addition of neoarsphenamine this is not true, since definite improvement continues during the second year.

SUMMARY

The clinical and serologic results obtained in 203 patients with various types of neurosyphilis after treatment with iodobismitol with saligenin alone and in combination with neoarsphenamine or tryparsamide are reported.

The therapeutic effect of iodobismitol with saligenin in patients with neurosyphilis is achieved rapidly and is not increased by prolonged administration. The effect, however, is definitely enhanced by the addition of either neoarsphenamine or tryparsamide, particularly the latter. Iodobismitol with saligenin is of value in the treatment of neurosyphilis, but it should not be used ordinarily as the only form of therapy.

EXFOLIATIVE DERMATITIS DUE TO NAPHTHALENE

REPORT OF AN ERUPTION RESEMBLING MYCOSIS FUNGOIDES

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There is a group of patients, frequently encountered by dermatologists, who have a dermatosis of a protean nature during the evolution of which there is always a phase which resembles mycosis fungoides or dermatitis herpetiformis. The eruption is further characterized by a tendency to clear up rapidly, especially during hospitalization, only to recur with equal rapidity when the patient returns to his usual environment. Sulzberger and Garbe [1] have collected and reported 9 cases of such a condition under the title "Distinctive Exudative Discoid and Lichenoid Chronic Dermatosis." Cannon [2] collected and reported 8 cases under the title "Allergic Dermatitis Simulating Lymphoblastoma." While an allergic basis for the conditions in these cases was surmised by Cannon from the clinical course, Sulzberger and Garbe could not find sufficient evidence to "consider this dermatosis as a representative form of any known atopic manifestation, although it may be some form of sensitization dermatosis."

I have observed a patient whose dermatosis fulfilled all the requirements of the condition described by these authors but in whose case I was able to find an allergen, naphthalene, the elimination of which was responsible for the disappearance of the process. The dermatosis resembled mycosis fungoides so closely that several competent dermatologists made that diagnosis clinically, and their impressions were strengthened by independent histologic reports on different pieces of tissue by Drs. Walter Highman and Fred D. Weidman suggesting that diagnosis. The elimination of naphthalene, ordinarily used in households as moth balls or flakes, from the patient's environment resulted in prompt recovery, which has lasted uninterruptedly for seven years.

REPORT OF A CASE

History.—X. Y., a physician aged 43, born in Russia, was in good health until October 1930. After a severe nervous strain due to the illness of his wife, some

1. Sulzberger, M. B., and Garbe, W.: Nine Cases of Distinctive Exudative Discoid and Lichenoid Chronic Dermatosis, Arch. Dermat. & Syph. **36**:247 (Aug.) 1937.

2. Cannon, A. B.: Allergic Dermatitis Simulating Lymphoblastoma, Arch. Dermat. & Syph. **39**:846 (May) 1939.

pruritic papules developed on the dorsal surfaces of his fingers and hands. They were rapidly followed by a generalized, profuse erythematosquamous eruption. There was severe itching accompanied by a burning sensation. Perspiration was profuse, especially at night. The slightest effort induced physical exhaustion, and the patient became irritable and apprehensive. His insomnia was persistent and yielded but slightly to sedatives. About six weeks after the onset of the eruption he entered a midwestern private sanatorium. Improvement began almost immediately after an operation for hemorrhoids. In the third week of his stay at the institution he suffered a mild relapse, consisting of itching, erythema and slight scaling. This attack was attributed to the eating of asparagus and to an unbalanced nervous mechanism. At the end of the fourth week he came home greatly improved. After the first night at home a progressive generalized eruption developed, for which he entered the Beth Israel Hospital in New York. Improvement began within twenty-four hours, and after three weeks he was sufficiently well to leave the hospital. Instead of returning home he went to stay with a relative in a nearby town. Within a day the itching, perspiration and scaling returned. On March 13, 1931 he entered the Newark Beth Israel Hospital, and again within a few days the acute symptoms subsided. He remained in the hospital five weeks. About two days after his return home exfoliation began again.

On April 25, through the kindness of Dr. Howard Fox, I saw this man for the first time and had him hospitalized in Mount Sinai Hospital in New York. The acute phase of the attack subsided in twenty-four hours. He was confined in this hospital for eight weeks. He then spent six weeks in the mountains of New York, where his recovery persisted. Two days after his return home he had an acute exacerbation. He was readmitted to the Newark Beth Israel Hospital in September, and his condition improved quickly. He stayed in the hospital nineteen weeks, after which he went to the seashore. His condition was unchanged for three days, but on the fourth day he sustained an acute exacerbation, coincident with the receipt of a trunkful of clothes from his home. He stayed on at the seashore and became progressively worse. In February 1932 he returned to the Newark Beth Israel Hospital. At that time his cutaneous condition was worse than it had ever been. However, improvement began immediately after admission and was continuous for two weeks, when a mild relapse lasting a few days occurred. This relapse followed contact with a pair of white duck trousers which were brought from home for the patient to wear in the hospital. A few hours after he put them on itching became intense, and new urticarial lesions appeared. Careful inquiry revealed that the trousers had lain several months in a drawer with naphthalene moth flakes. Contact tests with naphthalene gave, within ten hours, an erythematous reaction accompanied by generalized pruritus and crops of urticarial lesions. This test was repeated on several occasions with similar results. The results of contact tests with numerous other substances were negative. The patient was discharged from the hospital May 25. For the past seven years there have been no relapses, and with the exception of the appearance of a few transitory itchy papules, his skin has been normal. He returned to his home and is actively engaged in his profession, but he carefully avoids naphthalene.

Clinical Examination.—In April 1931, when I first saw this man, he presented a generalized erythematous eruption with exfoliation in large flakes. The palms, soles and mucous membranes were exempt. There were also a few scattered areas free from eruption on the chest and back. On the face, neck, chest, back and dorsal surfaces of the hands were brownish red infiltrated nodules, 5 to 30 mm. in size. There was generalized enlargement of the lymph nodes, especially noticeable

in the inguinal regions. The chest was emphysematous, with the heart enlarged to the right, and the liver was palpable about 2 fingerbreadths below the costal margin. The blood pressure was 110 systolic and 76 diastolic.

Laboratory Examinations.—Numerous examinations of the blood showed eosinophils ranging from 10 to 38 per cent. There was usually leukocytosis, but the erythrocytes and hemoglobin were within normal limits. The chemical examination of the blood gave normal results. Examination of the stools showed no parasites. Contact or patch tests with numerous substances obtained from his home all gave negative results with one outstanding exception, naphthalene moth flakes.

Roentgen ray examinations of the lungs showed moderate emphysema and thickened pleura of the right lung; it was also noted that the heart was enlarged to the right and that the aorta was sclerotic and moderately dilated. Roentgenograms of the teeth showed no apical infiltrations; those of the gastrointestinal tract revealed appendicular stasis lasting beyond the fourth day. The gallbladder was not definitely visualized, and examination of the bile gave essentially negative results. No arsenic was found in the urine.

Histologic Examination.—Dr. Fred D. Weidman on March 4, 1932, wrote as follows:

"The changes shown in the section are compatible with those of granuloma fungoides, and I can understand how the lesion could be that of mycosis fungoides, as it is understood at present dermatologically. By that I mean that there is a large group of cutaneous vices which will probably some day be shown to have the capacity of inducing the anatomic changes of that disease. I know of at least 1 case in which the cutaneous mycosis fungoides turned out to be Hodgkin's disease at necropsy, and it is probable that other vices of the reticuloendothelial system also have the power to produce dermatologic mycosis fungoides.

"The histologic features which are of value in corroborating Dr. Schamberg's diagnosis consist in, first, the high grade hyperplasia and edema of the epidermis, resulting in such a uniform swelling of epidermal pegs that their normal distribution and relations are scarcely disturbed. Secondly, the round cell infiltration of the corium is of sufficient grade to qualify as granuloma fungoides.

"There are two shortcomings for a diagnosis of granuloma fungoides; first, the absence of round cell infiltration of the epidermis (so-called abscesses of Pautrier), which is not so important, and, secondly, the comparative uniformity of the round cell types concerned in the infiltration. Thus, whereas there are moderate numbers of eosinophils present, the remaining cells are almost exclusively of a plasma cell type. This makes me wonder whether they might be myelocytes or perhaps cells of myeloma. Incidentally, the establishment of either of these conditions in a patient would not vitiate the sense of granuloma fungoides dermatologically but only amplify and substantiate suspicions that have been entertained a long time."

Dr. Walter Highman examined a different biopsy specimen made a year later and rendered the following report:

"With eosin and hematoxylin stain and low power magnification, the epidermis is surrounded by a moderately thick continuous scale, presenting numerous islands of parakeratosis. Below this there is a moderately thickened but not continuous granular layer, in places consisting of six or eight rows of cells. The entire system of rete pegs is almost uniformly three or four times its normal depth, with some of the pegs narrow and tonguelike and others fused together in groups of four or five, uniformly or enclosing areas of islands or tips of the papillae. The papillary

body is correspondingly changed in contour and presents a definite but not dense infiltration. The entire level of the subpapillary plexus presents a similar infiltration, which consists of dense foci, prevailingly circular or oval, lying in the background of sparse infiltration and edematous collagen. The area involved is the upper half of the cutis. The subcutaneous tissue is virtually without abnormalities.

"With high power it is seen that the cells of the suprapapillary rete are separated from one another by slightly exaggerated intercellular spaces showing stretched epithelial threads. This change becomes more marked in the pegs and is most definite nearest the basal layer. The basal membrane is intact. Nevertheless, throughout the pegs wandering cells are found, which apparently have migrated and which are chiefly from the tips of the papillae. A great many mitotic figures are seen in the pegs. The papillae present great numbers of dilated capillaries engorged with red blood cells. Around these capillaries are seen fibroblasts, lymphocytes and eosinophils in fairly even mixture and plasma cells, from 4 to 10 per field. The infiltration at the subpapillary level looks like that in the papillae, where it is diffuse, except that there is a greater number of plasma cells. The denser or focal areas appear clustered in dilated lymphatic spaces, are richer in fibroblasts and plasma cells and present a constant but not great number to the field of a large cell. This cell has a body somewhat irregular in outline and tends to have one or more angles, sometimes even one or two fine prolongations of the cytoplasm. A not great but definite amount of cellular detritus is seen. Here and there are large cells with two nuclei, which appear to be something more than merely fused round cells. A certain number of dividing cells are seen.

"The picture is one of a chronic scaling dermatitis, with a sluggish infiltration, highly variegated in its cellular elements and suggestive of activity in the lymphatic system, such as is seen in mycosis, although no positive opinion that this condition is mycosis can be expressed. A slide from the Mount Sinai Hospital dating from an earlier period is similar in composition."

Clinical Course and Treatment.—As has been stated in the history, the clinical course was characterized by periods of exacerbation and remission. One is struck by the fact that the exacerbations usually followed the patient's return home, and the acute symptoms always subsided quickly on admission to hospital. Many plans of treatment were carried out. Among these were injections of sodium thiosulfate, splenic extract, calcium gluconate and strontium bromide and the use of autohemotherapy, superficial roentgen therapy, restricted diets, colonic irrigations, baths, powders and bland ointments. During remissions the skin did not entirely return to normal. The exfoliation disappeared, and the skin became soft and pliable, but crops of urticarial lesions continued to appear, especially about the abdomen and neck. Some of these lesions were persistent, lasting for months. This was particularly true of those on the abdomen and on the backs of the fingers. Itching became less marked but interfered with sleep at night. The appetite was usually good. It was thought for a long time that the acute exacerbations on the patient's return home could be explained by an intense psychic strain produced by nervous tension, but there was little to support this theory.

The earliest case that I could find recorded in which naphthalene affected the skin was reported by Evers [3] in 1884. In this case there were nausea, abdominal pains, anorexia, insomnia, sweating and pruritus.

3. Evers: Erkrankung, anscheinend herforgerufen durch Naphthalin, Berl. klin. Wchnschr. **21**:593 (Sept. 15) 1884.

The condition resulted from naphthalene dusted on furniture. Several cases of poisoning from naphthalene are reported in children who had eaten moth balls.[4] Symptoms were those pointing to involvement of the nervous system, such as staggering gait, mental dulness, burning sensation in the urethra, nausea and vomiting. Ocular lesions have been produced in rabbits [5] and in human beings [6] by the administration of naphthalene. Recently Touraine and Ménétrel [7] described several cases of various dermatoses in workers exposed to hot naphthalene and to its chlorine derivatives. The chloronaphthalenes are used chiefly as waterproofing agents and may produce acne in workers exposed to their fumes.

Naphthalene is a product of the distillation of coal tar. The tar contains about 6 per cent of it. It is a hydrocarbon of the formula $C_{10}H_8$, known also as tar camphor, white tar or naphthalin. It occurs as white crystalline flakes or powder and has a strong coal tar odor. It melts at 80 C. and boils at 217.9 C. It is moderately volatile at ordinary temperature. It is insoluble in water but soluble in absolute alcohol, ether and benzene. It is used chiefly in the manufacture of dyes and as a moth repellent in households.

COMMENT

The ultimate result in this case, if the precipitating cause of the eruption had not been determined, cannot be foreseen, but it is interesting to speculate. The damage to the patient's reticuloendothelial system could have been carried to such an extent that true mycosis fungoides, or possibly Hodgkin's disease, might have developed, owing to repeated insults to that system. I purposely refrained from reporting this case at an earlier date, because I was so impressed with the clinical diagnosis of granuloma fungoides that the positive reactions to naphthalene were not too convincing at the time. Seven years has elapsed without any recurrence, and I feel that mycosis fungoides can

4. Peterson, F.; Haines, W. S., and Webster, R. W.: Legal Medicine and Toxicology, Philadelphia, W. B. Saunders Company, 1923. Zangerle: Therap. Monatsh. **13**:122, 1899; cited by Peterson, Haines and Webster, p. 694. Nash, L. F.: Naphthalene Poisoning, Brit. M. J. **1**:251, 1903; cited by Peterson, Haines and Webster, p. 694.

5. Michaïl, D., and Vancea, P.: Sur la multiplicité des voies par lesquelles on peut produire des lésions oculaires naphtaliniques, Compt. rend. Soc. de biol. **96**:63-65, 1927.

6. Lewin, L., and Guillery, H.: Die Wirkungen von Arzneimitteln und Giften auf das Auge: Handbuch für die gesamte ärztliche Praxis, Berlin, A. Hirschwald, 1905, vol. 1, p. 696.

7. Touraine, A., and Ménétrel, B.: Dermatoses professionnelles par la naphthalène et ses dérivés, Prat. méd. franç. **15**:335-346 (May, B) 1934.

be definitely excluded. The prompt and lasting recovery on elimination of naphthalene from the patient's environment points definitely to that agent as the causative factor in this case.

SUMMARY

Previous writers have described dermatoses resembling lymphoblastomas, which they surmised were of allergic origin. My case of naphthalene dermatitis resembling mycosis fungoides clinically and histologically suggests that the connecting link between surmise and fact has been established.

This case suggests that more careful allergic study be made in proved as well as suggestive cases of lymphoblastomas, especially those with a history of remissions while the patient was hospitalized.

PEMPHIGOID ERUPTION ASSOCIATED WITH HEMORRHAGIC NEPHRITIS FOLLOWING BISMUTH THERAPY

REPORT OF A CASE

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AND
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The constant introduction of new bismuth compounds [1] into syphilotherapy makes it necessary to call attention to dangerous complications from well established forms of bismuth medication, in order that physicians may not lose sight of these unusual but grave potentialities. We have had the opportunity of studying a patient with a generalized bullous eruption and hemorrhagic nephritis following the use of bismuth, which because of the rarity of these manifestations was deemed worthy of reporting.

Müller,[2] Boas [3] and Langer [4] mentioned that "bullous exanthems" may occur after the administration of bismuth, but they gave no details and apparently no references to reports of cases. Juliusberg [5] mentioned that Müller has reported a bullous eruption of the type of dermatitis herpetiformis, but in the references which were available to us we were unable to find such a report. The only reference [6] which we could not obtain might well have contained the description of this case.

From the Department of Dermatology and Syphilology, John H. Stokes, M.D., Director, and the Department of Medicine, O. H. Perry Pepper, M.D., Director, Hospital of the University of Pennsylvania.

1. (*a*) Meininger, W. M., and Barnett, C. W.: The Treatment of Syphilis with Sobisminol Mass Given by Mouth, J. A. M. A. **113**:2214-2218 (Dec. 16) 1939. (*b*) Scholtz, J. R.; McEachern, K. D., and Wood, C.: Sobisminol Mass: Clinical Results with Oral Administration, ibid. **113**:2219-2223 (Dec. 16) 1939.

2. Müller, H.: Wismutbehandlung der Syphilis, Zentralbl. f. Haut- u. Geschlechtskr. **7**:289-300, 1922.

3. Boas, K.: Ueber toxische Hauterscheinungen im Verlaufe der Wismutbehandlung der Syphilis, Med. Klin. **20**:1571-1573, 1924.

4. Langer, E.: Die Nebenerscheinungen bei der Wismutbehandlung der Syphilis, Klin. Wchnschr. **7**:554-559, 1928.

5. Juliusberg, F.: Die Nebenwirkungen der Wismutbehandlung, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol. 18, pp. 465-466.

6. Müller, H.: Weitere Versuche der Syphilisbehandlung mit Wismut, München. med. Wchnschr. **69**:1659, 1922.

We could find no mention of eruptions of this type in either the French or the English literature. The nearest approach to such a condition was in a report by Catzeflis,[7] who described a patient with a bullous eruption of the forearms and hands in association with severe pain, redness and swelling of the involved parts and erythema of the abdomen.

Hemorrhagic nephritis, in contrast to toxic nephrosis, is similarly a most unusual complication of bismuth medication. Many investigators, among whom are Fournier,[8] Gaté,[9] Dowds,[10] Schröder,[11] Leff [12] and Galliot,[13] who discussed the nephritic effects of this drug did not even mention this type of reaction. Others, i. e., Bory [14] and Eitzen,[15] stated that at times a few red cells may appear in the urine in connection with a bismuth toxic nephrosis.

On the other hand, Galliot [16] reported a fatal case of hemorrhagic nephritis in association with purpura, while Gawalowski [17] and Dassen and Rey [18] described instances in which hemorrhagic diarrhea and stomatitis occurred in conjunction with the hemorrhagic nephritis. Bory [14] mentioned that Nichols reported a case of hemorrhagic nephritis following administration of bismuth in a patient with "hypertensive Bright's disease."

Most writers seemed to feel that the hemorrhagic nephritis was simply an expression of a local purpuric condition of the kidneys most likely accompanied by toxic nephrosis rather than a true hemorrhagic nephritis.

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7. Catzeflis, A.: A propos de trois préparations bismuthiques; tartrobismuthate de soude et de potasse, luatol, et iodobismuthate de quinine, Ann. d. mal. vén. **19**:265-270, 1924.

8. Fournier, A.: Accidents de la bismuthérapie, Marseille méd. **63**:1718-1733, 1926.

9. Gaté, M. J.: Les accidents de la médication bismuthique dans le traitement de la syphilis, Vie méd. **8**:357-359, 1927.

10. Dowds, J. H.: Poisoning by Sodium Bismuth Tartrate Injections, Lancet **2**:1039-1040, 1936.

11. Schröder, P.: Ueber Nierenschädigungen bei der Wismutbehandlung bei Syphilis, Zentralbl. f. inn. Med. **52**:498-501, 1931.

12. Leff, C. O.: Chronic Bismuth Poisoning, Mil. Surgeon **70**:456-461, 1936.

13. Galliot, A.: La bismuthothérapie: Incidents, accidents, intolérance, J. de méd. et chir. prat. **106**:639-644, 1935.

14. Bory, L.: Néphrites bismuthiques, Paris méd. **1**:221-227, 1931.

15. Eitzen, A. C.: Toxic Effects of Bismuth, with Especial Reference to Renal Damage and Report of a Case of Anuria, Am. J. Syph., Gonor. & Ven. Dis. **21**:674-678, 1937.

16. Galliot, A.: Mort par néphrite hémorrhagique au cours d'un traitement bismuthé, Bull. Soc. franç. de dermat. et syph. **34**:174-176, 1927.

17. Gawalowski, K.: Therapeutic Intoxication with Bismuth, Česka dermat. **8**:241-244, 1927.

18. Dassen, R., and Rey, J. C.: Intoxicación aguda por el bismuto, Semana méd. **2**:1152-1156, 1930.

REPORT OF CASE

L. B., a Negress aged 39, was first seen on June 18, 1936.

Her husband had received a series of injections "for his blood" three years previously. The patient had never been pregnant, although she had been married fourteen years. There was a history of several attacks of "hives" many years before and of a tonsillectomy in her youth for recurrent sore throats. No evidence of constitutional or allergic diseases could be elicited either in the family history or in her past history.

Between October 1933 and March 1936 she received about forty-five "arm injections for bad blood." At some time during this period she received six injections in the buttocks. About nine months before her treatment terminated she had suffered nausea, chills and fever, but she was unable to state whether these symptoms occurred at the time of the intramuscular or the intravenous therapy. At any rate, it was quite clear that the patient tolerated the "arm treatments" without difficulty during he last nine months of the treatment.

A physical examination gave completely negative results. The Kahn and Kolmer serologic reactions and the result of an examination of the spinal fluid were reported as normal.

Treatment was begun on July 10, 1936, with intramuscular injections of 2 cc. of bismuth subsalicylate in oil (120 mg. of bismuth).

After both the fifth and the sixth injection the patient complained of itching, nausea, bad taste and headache, but after two weeks of rest the itching had almost entirely disappeared. The seventh and the eighth injections were tolerated well, but after the ninth and tenth treatments (October 16) the itching again became aggravated, and there developed a severely pruritic eruption, consisting of papules and vesicles scattered over the arms and the thighs and an erythematous edema involving the eyelids, the sides of the neck and the volar aspect of the left forearm. Bismuth medication was permanently discontinued.

By November 2 the eruption had become generalized and was strikingly polymorphous, and the vesicular and bullous phases were more pronounced. Ten days later the patient had become febrile and was ill enough to be admitted to the Hospital of the University of Pennsylvania.

At the time of her admission the patient presented an extensive generalized eruption consisting of erythematous, urticarial, vesicular and bullous lesions, of which some were grouped, some confluent and others discrete. Many of the lesions were oozing. Some of them presented annular and gyrate configurations. The face was the least involved, but the eyelids were swollen and the lips were studded with vesicles. Similar lesions were found at the angles of the mouth. The neck was heavily involved with erythematous patches and vesicular lesions. The extremities were swollen and tender and were the sites of confluent, oozing, eczematoid lesions, as well as erythematous, papular, vesicular and bullous lesions. On the trunk many of the lesions were urticarial, with superimposed vesicular and bullous elements.

Examination of the mouth revealed many filled and several capped teeth. The remainder of the physical examination gave negative results. The blood pressure was 120 systolic and 70 diastolic.

By November 15 the eruption had changed somewhat. Nearly all the elementary lesions had become large, clear, serous bullae, which arose from what appeared to be normal skin, but within one week they became hemorrhagic, and at the same time hemorrhagic erosive lesions formed in the nasal chambers and on the lips. This severe hemorrhagic phase continued for about five days, after which the patient's cutaneous condition began to improve.

During the first two weeks in the hospital the patient's general condition became gradually worse. She suffered greatly with nausea and frequent vomiting. There then ensued increasing weakness, dyspnea, abdominal distention and frequency of urination. The temperature by mouth ranged irregularly between 97 and 102 F., while the pulse and respiratory rates were more or less commensurate with the febrile changes.

Between December 1 and December 8 the patient was acutely ill. Although the temperature range remained about the same, the pulse and respiratory rates became rapid: 100 to 140 for the former and as high as 48 for the latter. At this time the patient complained of substernal pain, dyspnea and cough, all of great severity. Many rales were easily heard over the areas of both lungs, anteriorly and posteriorly. The picture was interpreted as diffuse bronchitis complicated by beginning cardiac failure. The rales disappeared in a few days but were succeeded by orthopnea, pallor, generalized edema and ascites. A gallop rhythm was present.

By December 4 it became evident that the patient also had acute nephritis. The urea nitrogen content of the blood had risen to 60 mg. per hundred cubic centimeters, and red cells, albumin and casts made their appearance in the urine. The blood pressure rose to 160 systolic and 100 diastolic.

Several days later symptomatic evidences of improvement commenced. The dyspnea gradually subsided; the edema began to disappear, and the urinary output increased. Within ten days the urea nitrogen content of the blood fell to 18 mg. per hundred cubic centimeters. All evidences of edema disappeared by December 29, and by Jan. 8, 1937, the blood pressure reading had fallen to 132 systolic and 82 diastolic. The temperature, the pulse rate and the respiratory rate gradually reached normal and remained at these levels.

The patient was discharged from the hospital on January 26 and was observed regularly at the renal disease and dermatologic clinics. For a number of months after discharge the urinalyses continued to show decreasing numbers of red cells. These eventually disappeared entirely. Urinalyses in the past two years have given normal results.

During the height of the eruption a culture of the fluid taken from a newly formed bulla and a culture of the blood were both sterile under both aerobic and anaerobic conditions. A culture of the urine showed a few hemolytic staphylococci, while a culture of the substance taken from the root of a tooth extracted just before the patient left the hospital showed two types of nonhemolytic streptococci and some diphtheroids.

The patient's serum was tested with several strains of stock hemolytic streptococci in the laboratory of Dr. Stewart Mudd by Dr. D. Sargeant Pepper, but no agglutinative power was demonstrated. Examination of the urine for bromides and iodides gave negative results on two occasions.

EXPERIMENTAL STUDIES

Vaccines were made with the organisms recovered from the extracted tooth and from the urine. A separate intracutaneous test of 0.1 cc. was made for each type of organism recovered. None of these showed immediate or delayed reactions which were significantly more pronounced than the reaction caused by a control injection of stock catarrhal vaccine.

A report on the analysis of the preparation of bismuth subsalicylate in oil used on this patient was obtained from the manufacturer,[19] who stated that it consisted of a suspension of bismuth subsalicylate in pure peanut oil. It contained in addition butyn 0.1 per cent and metaphen 1 : 10,000.

TABLE 1.—*Intracutaneous and Passive Transfer Tests*

	Intracutaneous Tests				Prausnitz-Küstner Tests*			
	Subject		Control		Subject		Control	
Substance Tested	20 Minutes	48 Hours	20 Minutes	48 Hours	20 Minutes	48 Hours	20 Minutes	48 Hours
Bismuth potassium tartrate (1 per cent)	14 by 13†	13 by 10	14 by 11	12 by 11	14 by 13	13 by 10	14 by 11	10 by 11
Neoarsphenamine (1 per cent)	12 by 8	7 by 8	11 by 11	8 by 7	11 by 10	7 by 8	10 by 12	8 by 6
Bismuth salicylate (1 per cent suspension)	7 by 5	3 by 3	8 by 6	8 by 6	6 by 4	3 by 3	8 by 6	7 by 5
Peanut oil	14 by 11	15 by 15	14 by 10	15 by 12	10 by 8	0	14 by 10	15 by 10
Butyn (1:1,000)	12 by 9	0	10 by 10	0	11 by 9	0	12 by 8	0
Metaphen (1:10,000)	8 by 8	6 by 6	11 by 11	6 by 5	12 by 8	6 by 6	11 by 9	6 by 5
Sodium salicylate (1 per cent)	8 by 8	2 by 2	11 by 19	2 by 2	11 by 8	2 by 2	11 by 8	2 by 2
Sodium tartrate (1 per cent)	13 by 9	2 by 2	11 by 8	2 by 2	11 by 9	2 by 2	11 by 8	2 by 2
Saline solution	8 by 9	0	10 by 10	0	8 by 11	2 by 2	10 by 11	0
Control serum	.....	.....	.....	.....	0	0	0	0

* Intracutaneous tests used as controls for Prausnitz-Küstner tests.
† Size of papules recorded in millimeters.

TABLE 2.—*Intracutaneous Tests with Compound Antigen* *

	Comp. Antigen Made with Subject's Serum				Comp. Antigen Made with Control Serum			
	Subject		Control†		Subject		Control†	
Substance Tested	20 Minutes	48 Hours	20 Minutes	48 Hours	20 Minutes	48 Hours	20 Minutes	48 Hours
Bismuth tartrate (1 per cent)	8 by 5	8 by 5	8 by 6	8 by 6	6 by 3	6 by 3	6 by 5	6 by 5
Neoarsphenamine (1 per cent)	0	0	0	0	0	0	0	0
Bismuth subsalicylate in oil	8 by 6	8 by 6	9 by 6	9 by 6	8 by 5	8 by 5	10 by 6	10 by 6
Peanut oil	0	0	10 by 13	10 by 13	0	0	11 by 14	11 by 14
Subject's serum	0	0	0	0	0	0	0	0
Control serum	0	0	0	0	0	0	0	0

* The antigen was made by incubating equal parts of the test substance and the serum for twenty-four hours at 37 C.
† The intracutaneous tests in table 1 were used as controls.

We obtained samples of each of these constituents from the manufacturer and with these proceeded to perform a number of patch, intracutaneous (table 1) and passive transfer tests (table 1), which were carried out in duplicate on the patient and a control subject.

19. This report was submitted to us by Dr. G. W. Raiziss, of the Dermatologic Research Laboratories in Philadelphia, a division of the Abbott Laboratories.

All these tests gave negative results in so far as they might demonstrate increased reaction capacity of the patient to the substances used.

Table 2 is an attempt to demonstrate the reactivity of the skin to a compound antigen, made by incubating a double strength concentration of the test substance with equal parts of the serum obtained from either the patient or the control subject. The mixture was incubated at 37 F. for twenty-four hours, and then 0.1 cc. was injected intracutaneously.

By a comparison of these figures with results obtained from the simple intracutaneous tests as recorded in table 1, which were used as controls, it is obvious that no effective compound antigen was demonstrated.

The degrees of reactivity noted were the same irrespective of the serum used.

COMMENT

Pemphigoid or bullous toxic eruptions, like other toxic manifestations of the skin, may be caused by widely different etiologic agents. Certain drugs, notably the iodides, phenolphthalein, aconite,[20] antipyrine and arsenic,[21] are well known for their tendency to produce this type of eruption in suitably sensitized persons. Recently the arsphenamines [22] have also been incriminated in this respect. A not inconsiderable number of writers have reported similar eruptions in association with severe constitutional disorders, such as malignant conditions [21] and acute infections.[23]

It is generally agreed that one cannot prove that a drug is the cause of a particular eruption unless one can reproduce the eruption by subsequent administration of the suspected drug.[24] Such a procedure in the case of mild cutaneous manifestations is indeed feasible and is constantly being utilized to prove the causation of these conditions.

In regard to severe and dangerous types of eruptions, such as that in our patient, one is hardly justified in attempting to reproduce a con-

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20. Fox, E. C.: Dermatitis Medicamentosa, Dallas M. J. **18**:138-139, 1932.

21. Elliot, J. A.: Bullous Dermatoses of Toxic Origin: Report of a Case Involving an Association with Choriocarcinoma, Arch. Dermat. & Syph. **37**: 219-233 (Feb.) 1938.

22. (*a*) Muir, K. B.: Vesiculobullous Dermatitis Following Administration of Arsphenamine: Case, Arch. Dermat. & Syph. **35**:226-230 (Feb.) 1937. (*b*) Raubitschak, F.: Bullöse Salvarsandermatose, Arch. f. Dermat. u. Syph. **175**: 114-116, 1937.

23. (*a*) Röper, C.: Bullöse hämorrhagische Dermatose bei Typhus, München. med. Wchnschr. **78**:2036-2037, 1937. (*b*) Baryer, E. S., and Matveev, S. G.: Vesico-Bullous Hemorrhagic Dermatitis in Human Undulant Fever, Sovet. vrach. gaz. **31**:631-632, 1932. (*c*) Jona, G.: Su due casi di affezioni bullose fibrili, Pediatria d. med. prat. **7**:94-102, 1932.

24. Abramowitz, E. W.: Cardinal Points in the Diagnosis of Drug Eruptions, M. Clin. North America **22**:1323-1331, 1938.

dition which on a previous occasion nearly resulted in the person's death. Abramowitz [24] stated, "If it is not safe to use even the smallest dose of the suspected drug, then future avoidance of the particular drug, with actual use of the other drugs taken as a control should finally determine the one which is responsible."

Such a procedure was adopted in the case reported here. After her recovery, the patient was given successively intramuscular injections of 2 cc. each of peanut oil, butyn 0.1 per cent and metaphen 1 : 10,000, with no ill effects. Furthermore, the patient was observed for a period of almost three years after her recovery, with no recurrence of her symptoms.

The difficulties of proving a drug to be the cause of an eruption are complicated by the fact that, although a drug may be responsible for the occurrence of a dermatitis on one occasion, at some later time administration of the drug may fail to reproduce the eruption. This situation seems to be particularly true of bismuth eruptions.[25]

It is, of course, well known that bismuth eruptions are much more common when there is previous or concomitant arsenical treatment than if a bismuth compound is administered alone.[25] It seems as if arsphenamine sets the state or primes the patient for reactivity to bismuth. Such might have been the situation with our patient.

By following the arsenic-free technic of Schoch [26] in the routine cleansing of our syringes, we feel that an arsenical played no direct role in precipitating this patient's eruption.

We were informed by the manufacturer that the bismuth compound which we used was free of any trace of arsenic, and this is borne out by reports in the literature,[27] which indicate that a great many bismuth preparations on the market today contain no trace of arsenic.

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25. (*a*) Sézary, A.: Les complications cutanées du traitement conjugé arsénobismuthique, Progrès méd. **44**:1891-1892, 1929. (*b*) Jordan, J. W., and Walker, H. L.: Dermatitis Due to Bismuth Compounds Associated with Cutaneous Sensitivity to the Arsenobenzols, New York State J. Med. **38**:483-488, 1938. (*c*) Skolnick, E. A., and Aleshire, I.: Skin Eruptions from Bismuth Therapy in Syphilis, J. A. M. A. **98**:1798-1801 (May 21) 1932. (*d*) Grund, J. C.: Bismuth Eruptions: Disorders of the Skin Following Intra-Muscular Administration of Bismuth Compounds in Treatment of Syphilis, Boston M. & S. J. **196**:996-1000, 1927. (*e*) Lortat-Jacob, L., and Roberti, J.: Les éruthrodermies bismuthiques, Médecine **8**:147, 1926.

26. Schoch, A. G.: The Patch Test and the Element of Syringe Contamination in Arsphenamine Sensitization Dermatitis, J. A. M. A. **98**:1367-1372 (April 16) 1932.

27. (*a*) Lowenburg, H., and Naide, M.: Arsenic Poisoning Caused by a Mouth Wash Containing Solution of Potassium Arsenite, J. A. M. A. **100**:737-738 (March 11) 1933. (*b*) Russel, E. R.: Presence of Arsenic in Bismuth Preparations, Arch. Dermat. & Syph. **28**:841-842 (Dec.) 1933.

It has been repeatedly demonstrated in the literature on drug eruptions that the ordinary patch, intracutaneous and passive transfer tests usually fail to show the presence of sensitivity. As one would expect, our results with these procedures were entirely negative.

In accordance with the fundamental work of Landsteiner [28] on conjugated antigens and its application by Rosenthal [29] to the experimental demonstration of the transfer of phenolphthalein sensitivity by means of a phenolphthalein conjugate, we attempted to demonstrate sensitivity to an incubated mixture of serum and bismuth which presumably might contain an appropriate compound antigen. These experiments all gave negative results.

Kenedy [30] reported that he was able to demonstrate the passive transfer of phenolphthalein sensitivity by performing the Prausnitz-Küstner test on a normal person who previously had ingested phenolphthalein. He stated the belief that the normal control subject elaborated the appropriate compound antigen, which in turn reacted with the antibodies in the serum of the sensitive person, thus resulting in a positive reaction.

It was because of Kenedy's work that we chose as our control subject a person who was receiving, but who showed no evidences of reactivity to, bismuth subsalicylate in oil. We, however, were unable to repeat Kenedy's results.

There is much evidence that this patient had true hemorrhagic nephritis rather than a purpuric manifestation with nephrosis. In the first place, the red cells appeared in the urine after the hemorrhagic phenomena in the skin and mucous membranes had disappeared. Furthermore, red cells as well as casts and albumin were found in the urine for several months after the patient's discharge from the hospital. At the time of the onset of the urinary changes there were not only anemia and increased blood urea nitrogen but also a rise in blood pressure.

It may be, as Bory [14] stated, that a toxic condition, such as this patient presumably had, may precipitate a potentially primed but latent hemorrhagic nephritis into activity. Stokes and Cathcart [31] have pointed out the role that infection plays in precipitating outbreaks of allergic

28. Landsteiner, K.: Specificity of Serological Reactions, Springfield, Ill., Charles C. Thomas, Publisher, 1936, p. 100.

29. Rosenthal, S. R.: The Conjugation of Haptens in Vivo: Phenolphthalein, J. Immunol. **34**:251-267, 1938.

30. Kenedy, D.: Sulla ipersensibilità alla fenolftaleina, Gior. ital. di dermat. e sif. **75**:965-968, 1934.

31. Stokes, J. H., and Cathcart, E. P.: Contributory Factors in Post-Arsphenamin Dermatitis, Arch. Dermat. & Syph. **7**:14-49 (Jan.) 1923.

character. Also, the biotropism of Milian [32] has been broadened to include this type of reactivity. For this reason, we studied the reactions to the intracutaneous injection of organisms which were cultured from the abscessed tooth and from the urine in the hope of demonstrating increased reactivity; but the results of the tests were all within normal limits. Similarly, the agglutination tests of the patient's serum to various strains of stock streptococci gave negative results.

SUMMARY

A case is reported in which a generalized bullous eruption and hemorrhagic nephritis followed bismuth therapy. In the literature no other case of a similar nature has been reported. Various tests to demonstrate objectively sensitivity to bismuth all gave negative results. Our reasons for believing that this patient's symptoms were due to reactivity to bismuth are discussed.

32. Milian, G., in Darier, J., and others: Nouvelle pratique dermatologique, Paris, Masson & Cie, 1936, vol. 4, p. 688.

A PROPOSED CLASSIFICATION OF CUTANEOUS LIPOIDOSES

WITH DESCRIPTION OF A NEW LOCAL LIPOID DERMATOSIS: IMBIBITIO LIPOIDICA COLLAGENI DEGENERATI CUTIS

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The lipoidoses, as one of us (E. U.) explained elsewhere,[1] are now classified in two large groups, namely, the general and the local lipoidoses. This division is based on demonstration of the fact that in the former there is a general, primary disturbance of fat metabolism, whereas in the latter there is a local disease of the tissue with secondary deposition of fat.

The general lipoidoses represent a process of fatty infiltration; their further classification is based on clinical type, the nature of the lipoid (cholesterol ester, free cholesterol, phosphatide, lecithin or kerasin), the intracellular or extracellular presence of the lipoid and the histologic features. The table presents a summary of these items.

The xanthelasmatoses (this term is preferable to xanthoma, because a blastomatous character is demonstrable only in extremely rare instances) can at present be classified only from a clinical point of view, because histologically and chemically no sharp differentiation is possible.

(1) Xanthelasma
  (a) xanthelasma localisatum (xanthelasma palpebrae and xanthelasma tumoriforme)
  (b) xanthelasma disseminatum
  (c) xanthelasma diffusum (cholesteroderma; complete infiltration of extensive areas)
  (d) xanthelasma generalisatum (including involvement of the mucosae and internal organs)
  Special type: Hand-Schüller-Christian syndrome.

(2) Xantheloid (formerly designated xanthofibroma and xanthofibrosarcoma)

(3) Xanthoma (xanthoblastoma)

The local lipoidoses are caused by primary local disease of the tissue of most varied nature (trauma, infection, intoxication or wear and tear), with a secondary deposition of lipoid in the involved tissue. We have earlier designated this process as "imbibition," in order to emphasize what will be discussed more fully, namely, that we have here to deal

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1. Urbach, E.: Lipoid Stoffwechselerkrankungen der Haut, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1932, vol. 12, p. 238.

with not lipoid degeneration of the connective or elastic tissue but impregnation of primarily diseased tissue with fatty substances excreted by the blood at this site. The question as to whether disturbed local fat metabolism or increased blood lipoid must be considered as a necessary prerequisite would have to be answered differently for the various local lipoid dermatoses; i. e., the blood lipoid is normal in cases of resorption

Proposed Classification of the Cutaneous Lipoidoses (Urbach)

Lipoidoses	Clinical Type	Type of Lipoidosis, as Regards Histologic and Chemical Nature	Chief Chemical Characteristics
General	Xanthelasmatosis (infiltration type)	Cholesterol cellular lipoidosis	Cholesterol ester and free cholesterol (ratio 2:1)
	Extracellular cholesterosis (Urbach, Epstein and Lorenn.[41] Kerl, W., in Jadassohn, J., and Zeller, K.: Ikonographia dermatologica, Berlin, Urban & Schwarzenberg, 1932)	Cholesterol lipoidosis	Free cholesterol and cholesterol ester (ratio 3:1)
	Niemann-Pick disease	Phosphatide cellular lipoidosis	Lecithin
	Hepatosplenomegalic skin and mucous membrane lipoidosis (Bürger, M., and Grütz, O.: Arch f. Dermat. u. Syph. **166**: 542, 1932)	Phosphatidic and phosphatide cellular lipoidosis	Phosphatides and cholesterols
	Lipoid proteinosis (Urbach, E., and Wiethe, C.: Virchows Arch. f. path. Anat. **273**: 585, 1929; Arch. f. Dermat. u. Syph. **168**: 94, 1933)	Phosphatidic lipoidosis	Lipoid-protein mixture, the former probably from the phosphatide group
	Gaucher's disease	Cerebroside cellular lipoidosis	Kerasin
Local	Xanthelasma (resorption type) (Urbach, E.: Klin. Wchnschr. **2**: 542, 1923)	Cholesterol cellular lipoidosis	Cholesterol ester and free cholesterol (ratio 2:1)
	Necrobiosis lipoidica diabeticorum (Urbach[42] and Oppenheim[45])	Lipoid imbibition of primarily necrotic cutaneous tissue	Lipoids not belonging to the cholesterol group
	Imbibitio lipoidica telae elasticae degeneratae	Lipoid imbibition of pathologically altered elastic tissue of the skin	Lipoids not belonging to the cholesterol group
	Imbibitio lipoidica collageni degenerati cutis	Lipoid imbibition of pathologically altered connective tissue of the skin	Lipoids not belonging to the cholesterol group

xanthelasma and imbibitio lipoidica telae elasticae degeneratae but increased in cases of necrobiosis lipoidica diabeticorum and of imbibitio lipoidica collageni degenerati cutis.

Among the local lipoidoses one also has to distinguish several diseases, as shown in the table, in part depending on the chemical aspects of the lipoids but predominantly, however, according to the tissues in which imbibition occurs (connective tissue, elastic tissue and necrotic tissue).

Certain objections have been offered to our classification. Andrews [2] has described it as "Slightly arbitrary, because the chemical nature of some of the lipoids is extremely complex and as yet not understood." He furthermore demurred that "There seems to be a mixture of several types." Weidman [3] most justly has stipulated that only the future will show whether this classification will prove merely transitory or permanent, for at the date of that criticism there had appeared few, if any, confirmations of the new disease pictures presented by one of us (E. U.), such as extracellular cholesterosis, lipoid proteinosis and necrobiosis lipoidica diabeticorum. Fortunately, in the meantime numerous writers from various countries have reported a large number of such cases; the most important of the writers are listed in the following tabulation.

Extracellular Cholesterosis

Laymon [4] } The articles refer
Montgomery and Osterberg [5] } to the same case

Lipoid Proteinosis

Benesi [6]	Wise and Rein [11]
Hoffmann [7]	Haxthausen [12]
Kindler [8]	Bazex [13]
Tripp [9]	Hansen [14]
Schreus [10]	

Necrobiosis Lipoidica Diabeticorum

Galewsky [15]	Monacelli [23]	Bernstein [32]
Balbi [16]	Kren [24]	Greenwood and Rockwood [33]
Gottron [17]	Connor [25]	Sweitzer and Laymon [34]
Zeisler and Caro [18]	Nicolau [26]	Fox [35]
Michelson and Laymon [19]	Klaber [27]	Wile and Belote [36]
Tannenholz [20]	Usher and Rabinowitch [28]	Rattner [37]
Goldsmith [21]	Jamieson [29]	Riehl [38]
Gross and Machacek [22]	Sweitzer [30]	Boldt [39]
	Hitch [31]	Schuermann [40]

2. Andrews, G. C.: Diseases of the Skin, Philadelphia, W. B. Saunders Company, 1938.

3. Weidman, F. D.: Position of "Pseudodiabetic Xanthoma" Among the Lipoid Disturbances of the Skin (Urbach), Arch. Dermat. & Syph. **35**:815 (May) 1937.

4. Laymon, C. W.: Extracellular Cholesterosis, Arch. Dermat. & Syph. **35**: 269 (Feb.) 1937.

5. Montgomery, H., and Osterberg, A. E.: Xanthomatosis, Arch. Dermat. & Syph. **37**:373 (March) 1938.

6. Benesi, O.: Zur Kenntnis der Lipoidosis cutis et mucosae (Urbach und Wiethe), Ztschr. f. Laryng., Rhin. u. Otol. **21**:60, 1931.

7. Hoffmann, E.: Lipoidosis cutis et mucosae, Dermat. Ztschr. **62**:296, 1931.

8. Kindler, W.: Beitrag zur Lipoidosis cutis et mucosae (Lipoidproteinose), Ztschr. f. Hals-, Nasen- u. Ohrenh. **30**:659, 1932.

9. Tripp, R. N.: Lipoidosis Cutis et Mucosae, New York State J. Med. **36**: 619, 1936.

10. Schreus, H. T.: Lipoidproteinose Urbach Wiethe, Zentralbl. f. Haut- u. Geschlechtskr. **53**:529, 1936.

(Footnotes continued on next page)

Nearly all these authors at the time of writing were of the opinion that the aforementioned lipoid dermatoses had been clearly defined histologically and clinically so as to justify their special designation and differentiation.

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11. Wise, F., and Rein, C. R.: Lipoidosis Cutis et Mucosae (Lipoid-Proteinosis of Urbach), Arch. Dermat. & Syph. **37**:201 (Feb.) 1938.

12. Haxthausen, H.: Lipoidosis cutis et mucosae (Urbach), Zentralbl. f. Haut- u. Geschlechtskr. **55**:514, 1937.

13. Bazex, A.: Un cas de lipoïdo-protéinose (Maladie de Urbach-Wiethe), Bull. Soc. franç. de dermat. et syph. **46**:136, 1939.

14. Hansen, P.: Ein Fall von Lipoidproteinose, Arch. f. Dermat. u. Syph. **175**:618, 1937.

15. Galewsky, E.: Nekrobiosis lipoidica diabeticorum (Urbach), Zentralbl. f. Haut- u. Geschlechtskr. **43**:252, 1933.

16. Balbi, E.: Ricerche intorno alla patogenesi della necrobiosis lipoidica diabeticorum Urbach-Oppenheim, Gior. ital. di dermat. e sif. **74**:14, 1933.

17. Gottron, H.: (*a*) Dermatitis atrophicans lipoides diabetica, Zentralbl. f. Haut- u. Geschlechtskr. **43**:721, 1933; (*b*) Zur Kenntnis und Pathogenese der Dermatitis atrophicans lipoides diabetica bzw. Nekrobiosis lipoidica diabetica, Med. Klin. **34**:145 and 190, 1938.

18. Zeisler, E. P., and Caro, M. R.: Nekrobiosis lipoidica diabeticorum, Arch. f. Dermat. u. Syph. **30**:796, 1934.

19. Michelson, H. E., and Laymon, C. W.: Necrobiosis Lipoidica Diabeticorum (Urbach): Dermatitis Atrophicans Lipoides Diabetica (Oppenheim), J. A. M. A. **103**:163 (July 21) 1934; Necrobiosis Lipoidica Diabeticorum, Arch. Dermat. & Syph. **35**:1130 (June) 1937.

20. Tannenholz, H.: Necrobiosis Lipoidica Diabeticorum (Urbach), Arch. Dermat. & Syph. **29**:931 (June) 1934.

21. Goldsmith, W. N.: Necrobiosis Lipoidica, Proc. Roy. Soc. Med. **28**:363, 1935.

22. Gross, P., and Machacek, G. F.: Necrobiosis Lipoidica Diabeticorum, Arch. Dermat. & Syph. **32**:491 (Sept.) 1935.

23. Monacelli, M.: A proposito di lipoidosi cutanee, Boll. sez. region. Soc. ital. di dermat. e sif (supp., Gior. ital. di dermat. e sif.), 1935, no. 3, p. 212.

24. Kren, O.: Necrobiosis lipoidica diabeticorum, Zentralbl. f. Haut- u. Geschlechtskr. **49**:581, 1935; **55**:186 and 614, 1937.

25. Connor, W. H.: Necrobiosis Lipoidica Diabeticorum, Arch. Dermat. & Syph. **34**:705 (Oct.) 1936.

26. Nicolau, S.: Ein Fall von Nekrobiosis lipoidica diabeticorum (Oppenheim-Urbach), Zentralbl. f. Haut- u. Geschlechtskr. **53**:373, 1936; **57**:578, 1938.

27. Klaber, R.: Necrobiosis Lipoidica Diabeticorum (Urbach-Oppenheim), Proc. Roy. Soc. Med. **27**:713, 1934; **30**:976, 1937.

28. Usher, B., and Rabinowitch, I. M.: Necrobiosis Lipoidica Diabeticorum, Arch. Dermat. & Syph. **35**:180 (Jan.) 1937.

29. Jamieson, R. C.: Necrobiosis Without Diabetes, Arch. Dermat. & Syph. **36**:912 (Oct.) 1937; Necrobiosis Lipoidica Diabeticorum, ibid. **38**:311 (Aug.) 1938.

30. Sweitzer, S. E.: Necrobiosis Lipoidica Diabeticorum, Arch. Dermat. & Syph. **37**:150 (Jan.) 1938.

(Footnotes continued on next page)

EXTRACELLULAR CHOLESTEROSIS

It was only in the consideration of extracellular cholesterosis that Montgomery and Osterberg [5] suggested its classification as a form of xanthelasma (xanthoma) or xantheloid (xanthofibroma). The four chief points of differentiation between extracellular cholesterosis and xanthelasmatosis, in order to make the distinction between them perfectly clear, are the following:

1. *Clinical Picture.*—The clinical picture and course of extracellular cholesterosis are characteristic. The disease begins as an exanthem in the form of an erythema exsudativum multiforme. In both cases hitherto described (Urbach,[41] Laymon [4] and Montgomery and Osterberg [5]) vesicular primary efflorescences were demonstrated clinically and histologically. To date such lesions have not been described in cases of xanthelasma or xantheloid.

2. *Histologic Picture.*—Histologic examination reveals changes in efflorescences only a few days old, as well as in apparently normal skin, indicating primary injury of the epithelium and vessels at a time when the rest of the cutaneous tissue has a normal histologic appearance. Besides this severe injury of the vascular endothelium, after staining with sudan the walls of nearly all the capillaries show brownish red deposits, which as yet show no double refraction. As, however, aciculae and specks appear in the vicinity of the brown-stained areas on addition

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31. Hitch, J. M.: Necrobiosis Lipoidica Diabeticorum (Urbach and Oppenheim), Arch. Dermat. & Syph. **36**:536 (Sept.) 1937.

32. Bernstein, J. C.: Necrobiosis Lipoidica Diabeticorum (Urbach), Arch. Dermat. & Syph. **36**:282 (Aug.) 1937.

33. Greenwood, A. M., and Rockwood, E. M.: Necrobiosis Lipoidica Diabeticorum, Arch. Dermat. & Syph. **35**:727 (April) 1937.

34. Sweitzer, S. E., and Laymon, C. W.: Necrobiosis Lipoidica Diabeticorum, Arch. Dermat. & Syph. **35**:967 (May) 1937.

35. Fox, H.: Necrobiosis Lipoidica Diabeticorum, Arch. Dermat. & Syph. **37**: 1072 (June) 1938.

36. Wile, U. J., and Belote, G.: Necrobiosis Without Diabetes, Arch. Dermat. & Syph. **38**:311 (Aug.) 1938.

37. Rattner, H.: Necrobiosis Lipoidica Diabeticorum, Arch. Dermat. & Syph. **38**:268 (Aug.) 1938.

38. Riehl, G., Jr.: Necrobiosis lipoidica diabeticorum, Zentralbl. f. Haut- u. Geschlechtskr. **57**:11, 1938.

39. Boldt, A.: Nekrobiosis lipoidica (diabeticorum), Arch. f. Dermat. u. Syph. **179**:74, 1939.

40. Schuermann, H.: Nekrobiosis lipoidica ("Diabeticorum") ohne Diabetes im Bereiche einer Purpura Majocchii bei Hypertonus, Zentralbl. f. Haut- u. Geschlechtskr. **62**:339, 1939.

41. Urbach, E.; Epstein, E., and Lorenz, K.: Extrazelluläre Cholesterinose, Arch. f. Dermat. u. Syph. **166**:243, 1932.

of digitonin at this time, it is assumed that the lipoid substances are formed chiefly from free cholesterol.

3. *Histochemical Picture.*—Histochemical examination reveals an almost exclusively extracellular, i. e., interfibrillar and intrafibrillar, distribution of the lipoid substances. This leading symptom is in no way invalidated by the fact that here and there a histiocyte may absorb lipoid, giving rise to foam cells.

4. *Chemical Findings.*—Chemical examination shows that the ratio of cholesterol fatty acid ester to free cholesterol in a xanthelasma nodule is 2:1; in extracellular cholesterosis the ratio is reversed, i. e., 1:3.

For all these reasons, we believe that the syndrome which we have named extracellular cholesterosis must be differentiated from xanthelasmatosis and xantheloid and must be presented as an independent entity.

NECROBIOSIS LIPOIDICA DIABETICORUM

In regard to the pathogenesis of necrobiosis lipoidica, opinions vary because some writers fail to attribute a determining significance to diabetes, as is done by Urbach.[42] Without entering into a polemical discussion, one of us (E. U.) wishes merely to draw attention to the fact that a normal result of a dextrose tolerance test does not necessarily exclude the former existence of diabetes. In this connection it must be recollected that xanthelasma may be associated with normal cholesterol content of the blood and that local myxedema of the skin may occur in hyperthyreosis.

For this reason, in cases of necrobiosis lipoidica with a negative result to a dextrose tolerance test, we recommend a determination of the sugar content of the skin or a cutaneous dextrose tolerance test (Urbach[43]).

It may be possible, however, that necrobiosis lipoidica can develop on other than a diabetic-toxic basis. According to Urbach, this disease is caused by damage of the walls of the blood vessels by toxic substances, with consequent local circulatory disturbances leading to necrobiosis. Owing to imbibition of the necrobiotic tissue with fat from the blood, there develops a secondary clinical picture of necrobiosis lipoidica. According to whether diabetes or other causes are responsible for these vascular changes, one may therefore speak of necrobiosis lipoidica diabeticorum or necrobiosis lipoidica of some other origin.

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42. Urbach, E.: (*a*) Beiträge zu einer physiologischen und pathologischen Chemie der Haut: X. Mitteilung. Eine neue diabetische Stoffwechseldermatose: Nekrobiosis lipoidica diabeticorum, Arch. f. Dermat. u. Syph. **166**:273-285, 1932; (*b*) Necrobiosis lipoidica diabeticorum mit Augenhintergrundveränderungen, Zentralbl. f. Haut- u. Geschlechtskr. **50**:281, 1935.

43. Urbach, E.: Zum Problem des isolierten hohen Hautzuckers bzw. Hautdiabetes, Klin. Wchnschr. **16**:452, 1937.

We are well aware of the difficulties associated with chemical confirmation of lipoid mixtures. However, in the presence of unequivocal and characteristic results, such as decided predominance of free cholesterol as compared with the predominance of cholesterol ester or the demonstration of phosphatides or lipoid-protein mixtures, these may even now be of value. These difficulties may become almost insurmountable if the diseased cutaneous areas are small, so that the biopsy specimen weighs only a few decigrams, as is the case with local lipoidoses. The histochemical methods are even less reliable, although a change in this regard may be brought about by the introduction of the use of fluorescence in microscopic technic.

In our opinion, there shortly will appear new lipoid dermatoses, differing clinically, histologically and chemically from those previously described. The disease which we herein describe is such a new lipoid dermatosis. It belongs to the so-called local lipoidoses and constitutes the fourth of this group that we have presented.

We understand the term "resorption xanthelasma" to mean a deposition of cholesterol fatty acid esters and free cholesterol in scars or otherwise injured cutaneous areas, associated with normal cholesterol metabolism. Whether in such cases the lipoid substances are liberated by the pathologic process in the tissue or are derived from the blood cannot at present be stated. Weidman [44] has contributed an excellent study of this problem.

With regard to necrobiosis lipoidica diabeticorum, differences in opinion might arise as to whether it would not more properly belong in the group of the general lipoidoses, because chemical analysis of the blood reveals hyperlipoidemia and hypercholesteremia; when, in spite of this, the lipoidosis is classified in the group of local lipoidoses, it is done in consideration of the outstanding symptom of necrobiosis, which in our opinion constitutes the primary basis for the local lipoid deposition. As is well known, there exists a wide difference between Oppenheim's [45] conception and our own; [42] Oppenheim has assumed that lipoid degeneration of the connective tissue is the cause of the yellow discoloration of the cutaneous lesions, whereas we assume that lipoid imbibition of the primarily necrotic tissue is the cause. We have introduced the working hypothesis of lipoid "imbibition" (deposition of lipoid substances in a tissue primarily injured from other causes), because the

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44. Weidman, F. D.: The Pathology of the Yellowing Dermatoses, Arch. Dermat. & Syph. **24**:954 (Dec.) 1931.

45. Oppenheim, M.: Ueber eine bisher nicht beschriebene, mit eigentumlicher lipoider Degeneration der Elastica und des Bindegewebes einhergehende chronische Dermatose bei Diabetes mellitus (Dermatitis atrophicans lipoides diabetica), Arch. f. Dermat. u. Syph. **166**:576, 1932.

pathologic anatomists, according to von Gierke,[46] refute the concept of lipoid degeneration of the connective and elastic tissues. Von Gierke wrote as follows: "The classification (fatty infiltration—fatty degeneration) corresponds to the theory that in infiltration the fat is carried from other parts of the body, but in degeneration is formed from decomposition of the cellular protein. This theory cannot be maintained, because we know now that also in fatty degeneration the fat is resorbed from the lymph current and because, on the other hand, it has not been possible to demonstrate any direct production of fat from protein in the animal or human body."

The significant difference lies only in the condition of the fat-containing cells; in the first case the condition is fatty infiltration of otherwise normal cells, whereas in the second case the condition is fatty infiltration of injured cells. In order to find expression for this in the nomenclature, one of us (E. U.) [42] once suggested that the term lipoid infiltration be used to designate fatty infiltration of otherwise normal cells or tissues and that the term lipoid imbibition be used to designate fatty infiltration of diseased or injured cells or tissues. We chose the latter designation because, as is well known, pathologically changed tissue shows a decided tendency to imbibe all manner of substances excreted by the blood, such as calcium, iron or pigment. Also, the designation fat phanerosis cannot be accepted. This term is meant to convey the rendering visible of previously dissolved or invisible and finely distributed fat substances by droplet precipitation or confluence. We rejected the term principally because the fat deposition in the diseased tissues is derived most probably from the blood fats and not from the locally liberated fat.

But quite apart from the fact that the conception of lipoid degeneration is not permissible from a pathologic anatomic standpoint, microscopic observation has shown that it would be most improbable in cases of necrobiosis lipoidica. With greater enlargement of specimens [47] stained with sudan, it can be shown that besides a diffuse brown staining of the basic substance, there is also striate or aciniform distribution of the lipoid droplets, which could be produced only by deposition of lipoid from without (via the blood stream) and never from local transformation of protein bodies into fatlike substances.

IMBIBITIO LIPOIDICA TELAE ELASTICAE DEGENERATAE

The same objections that we presented to Oppenheim's conception of necrobiosis hold good here with relation to a disease picture which

46. von Gierke, E.: Störungen des Stoffwechsels in Aschoff, L.: Pathologische Anatomie, Jena, Gustav Fischer, 1919, vol. 1, p. 429.

47. Urbach,[42a] fig. 7, p. 280.

Kreibich [48] has named "lipoid degeneration of the elastin." We have been able to demonstrate rather that one has here to deal with a primary severe lesion of the elastic tissue, usually of the face or neck (due to senility, light or exposure), which assumed secondarily a yellow color due to deposition of locally liberated lipoids. For these reasons we have suggested the designation "imbibitio lipoidica telae elasticae degeneratae." [49] This constitutes not so much a special clinical entity as a peculiar pathologic anatomic condition of various cutaneous lesions associated with a primary degeneration of the elastic tissues.

IMBIBITIO LIPOIDICA COLLAGENI DEGENERATI CUTIS

In the following pages are described a new local lipoid dermatosis which we have named "imbibitio lipoidica collageni degenerati cutis." As can be gleaned from this name, the condition this time is lipoid imbibition that involves exclusively primarily diseased cutaneous connective tissue, whereas in the foregoing paragraphs we considered a disease that involved only the elastic tissue and in necrobiosis lipoidica diabeticorum, primary local necrosis of all elements of the skin.

REPORT OF CASES

CASE 1.—V. W.,[50] an obese white woman aged 52, had about a dozen indurated lesions of diversified appearance on the external lateral surfaces of the arms, thigh and legs. The latest lesion, which had been present on the external aspect of the left tibia for three years, was about 4 mm. in diameter, elevated, hard and reddish brown. The other lesions, varying in duration from ten to thirty years, were of three types. All were definitely situated in the deeper part of the cutis, the skin over them being depressed and violet brown; they had a cartilaginous feel. Other lesions, likewise situated deeply in the cutis, presented an elevated keloid-like surface. Two lesions (above the right anterior iliac spine and on the left thigh) differed from all others in that they were yellowish brown but on pressure became distinctly yellow. Clinically, these lesions resembled necrobiosis lipoidica diabeticorum. The patient had rheumatism at the age of 13, and after that she had five attacks about five years apart. As a rule the attacks were limited to one joint, which became red and swollen, requiring rest in bed for one month for relief. A tonsillectomy was performed nineteen years previously. The first lesion (on the left hip) appeared thirty years ago, apparently associated with the rheumatic attack. The other lesions appeared on the arms, legs and thighs at various intervals, usually about five years apart, the last three years ago. None of the later lesions seemed to be related to the rheumatic infection. There was no history of preceding trauma. The blood pressure was 130 systolic and 70 diastolic. The peripheral arteries showed no beading or abnormal tortuosity. Except for slight

48. Kreibich, C.: Ueber lipoide Degeneration des Elastins der Haut, Arch. f. Dermat. u. Syph. **116**:325, 1913.

49. Urbach, E.: Imbibitio lipoidica telae elasticae degeneratae, Acta dermat.-venereol. **15**:69, 1934.

50. Presented at a meeting of the Philadelphia Dermatological Society, May 19, 1939 (Arch. Dermat. & Syph. **41**:180 [Jan.] 1940).

arteriosclerotic changes in the vessels, the eyegrounds appeared normal. The blood tests for syphilis gave negative results and the basal metabolic rate was +4 per cent. There were 5,000,000 red blood cells per cubic millimeter, with 7,200 white blood cells per cubic millimeter. Dextrose tolerance tests gave the following results:

Fasting	94
Half hour after ingestion of 100 Gm. of dextrose	164
One hour after ingestion of 100 Gm. of dextrose	121
Two hours after ingestion of 100 Gm. of dextrose	104

For certain reasons only the blood serum of the patient was examined for cholesterol at the first examination:

Total cholesterol	362 mg. per hundred cubic centimeters
Ester cholesterol	227 mg. per hundred cubic centimeters
Free cholesterol	135 mg. per hundred cubic centimeters

Immediately thereafter the patient was given a fat-free diet. The second determination of the principal lipoid components was made three weeks later. The results of lipoid analysis [51] of the blood serum at this time, compared with normal values are as follows:

	Patient's Values Mg. per 100 Cc.	Normal Values Mg. per 100 Cc.
Total lipoid	749	570 to 820
Neutral fat	200	100 to 200
Total fatty acids	413	190 to 420
(a) Phospholipid fatty acids	93	115 to 220
(b) Cholesterol ester fatty acids	131	64 to 88
(c) Neutral fat fatty acids	189	10 to 170
Total cholesterol	279	150 to 200
Ester cholesterol	196	90 to 130
Free cholesterol	83	70 to 90
Phospholipid phosphorus	5.6	7 to 14
Phospholipid as lecthin	140	175 to 330

It is clear that the original cholesterol level was considerably higher and was rapidly and greatly influenced by the fat-free diet. It also may be concluded, therefore, that the values of other fat components, all of which were found at the upper limits of normal, were probably increased before institution of the fat-free diet.

As the histologic findings in this case are identical with those in the second case, they will be considered with the latter.

CASE 2.—S. B., an obese Italian woman aged 48, was admitted to the hospital because of pruritus vulvae, which had been present for seven to eight years. The menopause occurred one year previously. On the external aspect of the upper part of the left arm was a yellowish red nodule about the size of a cherry, which, according to the patient, had been present for about thirty-seven years and had developed after vaccination. She was certain of this because she remembered that the nodule had itched and she had scratched it. The blood sugar value was 107 mg. per hundred cubic centimeters. Blood tests for syphilis gave negative results.

51. Total cholesterol was determined by Bloor's method. Ester cholesterol was determined by Bloor's method. Phospholipid was determined by the Fiske-Subbarow method. Fatty acids were determined by Stoddard and Drury methods. All other values were calculated from these values, as described by E. M. Boyd (The Oxidative Micro-Estimation of Blood Lipids, Am. J. Clin. Path. [Tech. Supp.] **2**:77, 1938).

The patient had suffered for fifteen years from pains in the upper part of the right side of the abdomen. The region of the gallbladder was sensitive to pressure.

The results of lipoid analysis of the blood were as follows:

	Patient's Values Mg. per 100 Cc.	Normal Values Mg. per 100 Cc.
Total lipoid	883	570 to 820
Neutral fat	325	100 to 200
Total fatty acids	540	190 to 420
(a) Phospholipid fatty acids	103	115 to 220
(b) Cholesterol ester fatty acids	128	64 to 88
(c) Neutral fat fatty acids	309	10 to 170
Total cholesterol	275	150 to 200
Ester cholesterol	192	90 to 130
Free cholesterol	83	70 to 90
Phospholipid phosphorus	6.8	7 to 14
Phospholipid as lecithin (lipoid phosphorus × 25)	155	175 to 330

Histologic Study.—Three nodules of various ages from case 1 (nodules of three, ten and thirty years' duration, respectively) and from the only tumor present in case 2, which was of thirty-seven years' duration, were studied histologically. The two last-mentioned tumors, which had persisted for at least three decades, presented identical pictures.

The most interesting and pathogenically the most important finding was that the histologic structure of all the tumors was practically the same except that in the younger nodules, of three to ten years' duration, no lipoid deposition could be demonstrated. From this finding the important conclusion may be drawn that the condition could not be a primary lipoid dermatosis but must be a local inflammatory lesion of the skin due to some other cause and proceeding to secondary lipoid absorption.

Hematoxylin-Eosin and Trichrome Stain.—More or less intense hyperkeratosis was present. The vessels in the stratum papillare cutis were dilated. Characteristic changes were seen in the connective tissue: In parts there appeared extraordinary proliferation of the connective tissue cells, with darkly staining nuclei and a striking diminution or condensation of the connective tissue fibrils (fig. 1). Among these, especially in the older nodules, there appeared abundant longitudinal cavities, which suggested that treatment of the sections with alcohol might have led to extraction of some substance, probably of a fatlike nature (fig. 2).

In other more deeply situated portions the connective tissue appeared condensed, consisting of irregular whorls (fig. 3).

The newly formed connective tissue showed extremely poor vascularization. The vessels that were present had thickened walls, with a swelling of the intimal cells.

Van Gieson's Stain.—Those areas which in the hematoxylin-eosin or trichrome specimens appeared rich in cells and nuclei after staining with Van Gieson's stain became greenish yellow instead of bright red. Furthermore, the normal gross fascicular structure of the connective tissue was lacking and was replaced by a fine linear whorl configuration.

Weigert's Stain.—This stain showed complete absence of elastic tissue, as regards both staining and structure in those portions of the skin which appeared yellow when the Van Gieson stain was employed.

Unna's Polychrome Methylene Blue Stain.—The pathologic components of the cutis appeared blue, indicating a so-called basophilic degenerated collagen or elacin, according to Unna.

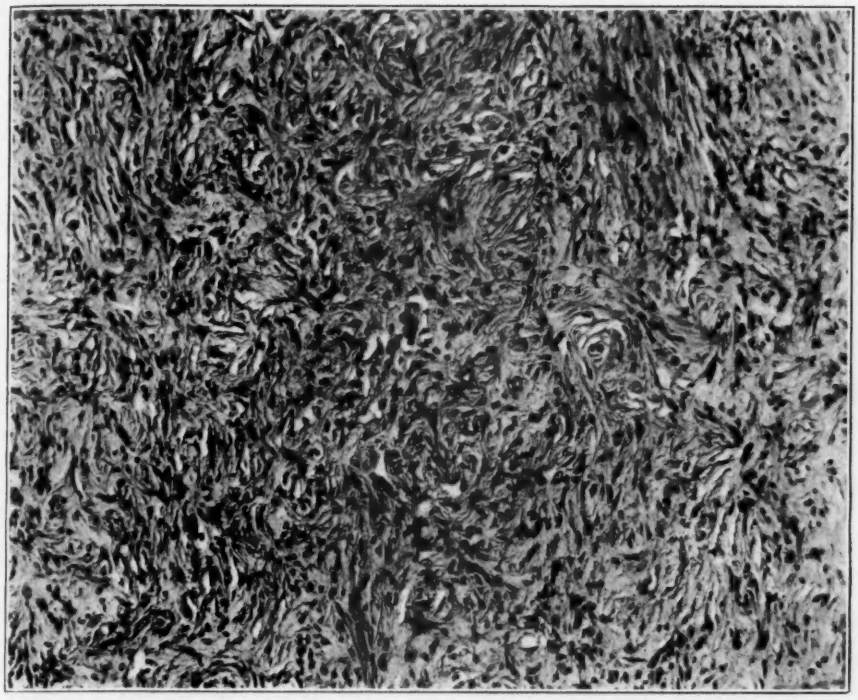

Fig. 1.—Extraordinary proliferation of the connective tissue cells, with darkly stained nuclei and condensation of the connective tissue fibrils (hematoxylin-eosin; × 132).

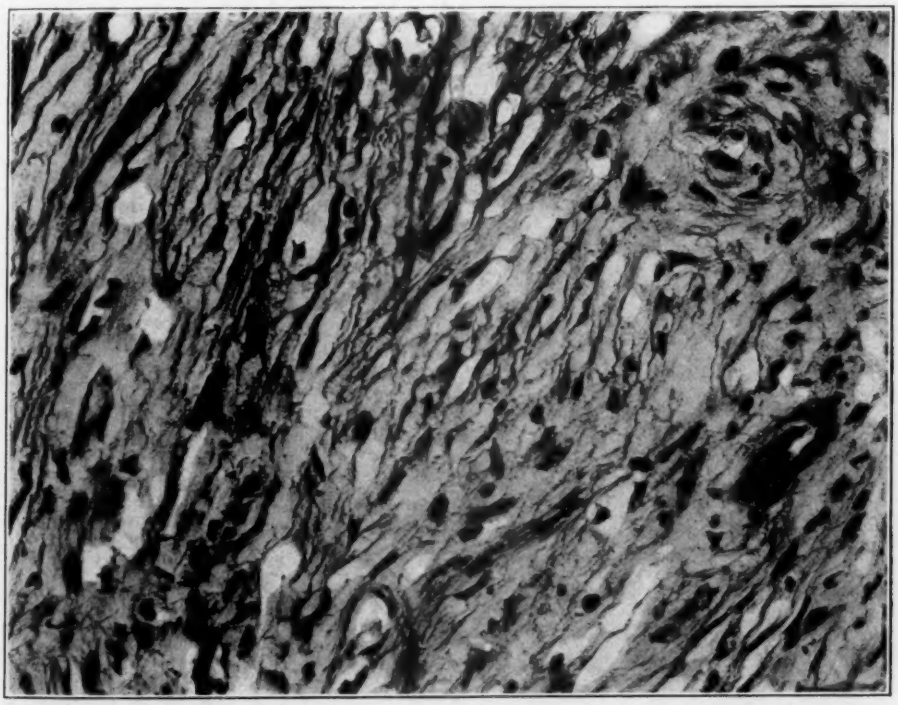

Fig. 2.—Abundant longitudinal cavities among the connective tissue fibrils, probably caused by extraction of a fatlike substance during the alcohol treatment of the sections (trichromic stain; × 450).

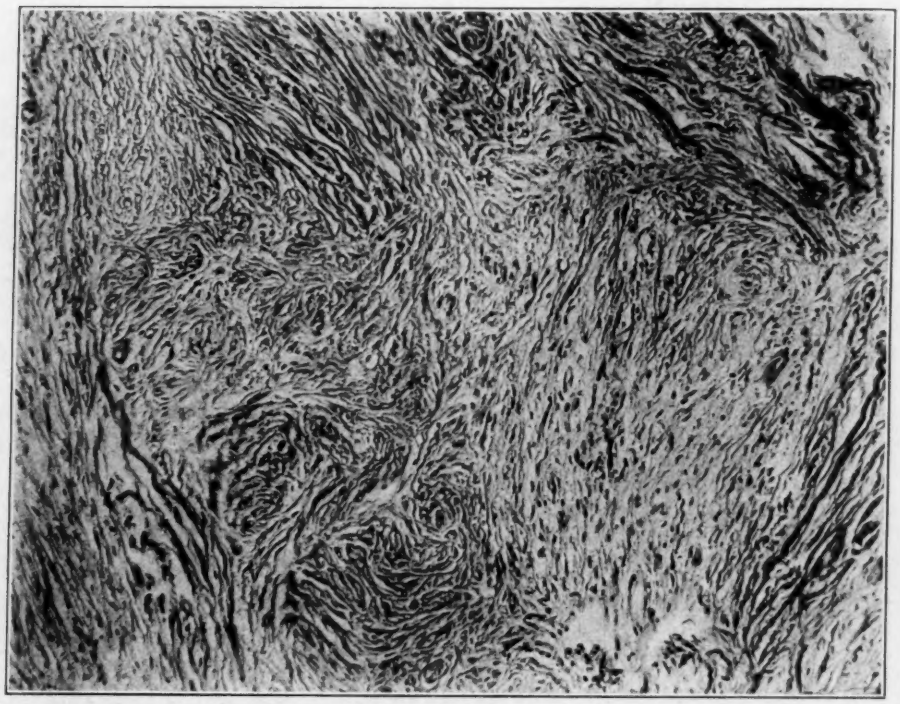

Fig. 3.—Condensed connective tissue arranged in irregular whorls (trichromic stain; × 132).

Fig. 4.—Brown-red masses in the stratum reticulare cutis (sudan IV stain; × 37).

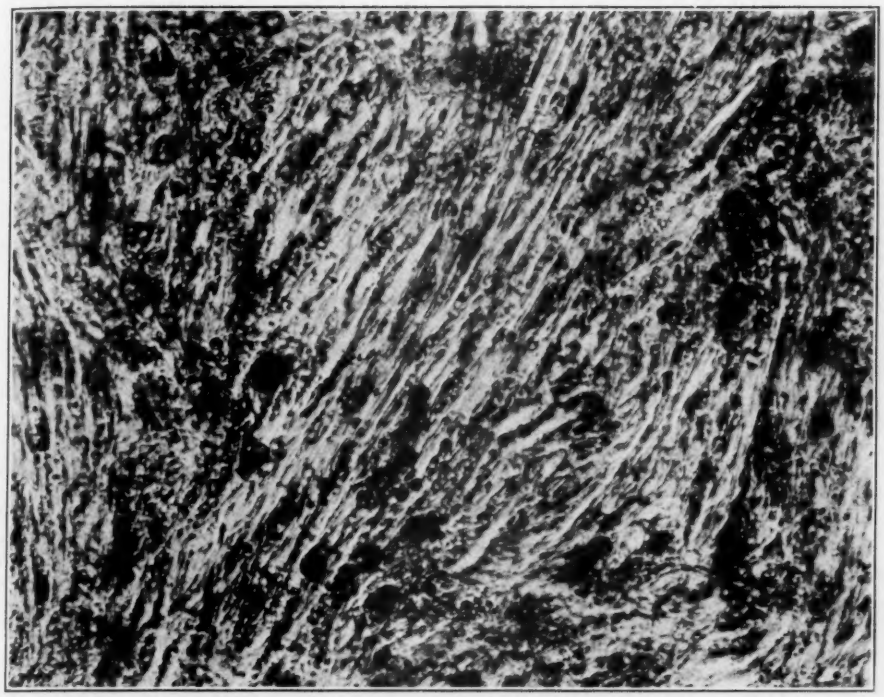

Fig. 5.—Globules and granules arranged in series especially between the fibrils of the connective tissue (interfibrillar) (sudan IV; × 450).

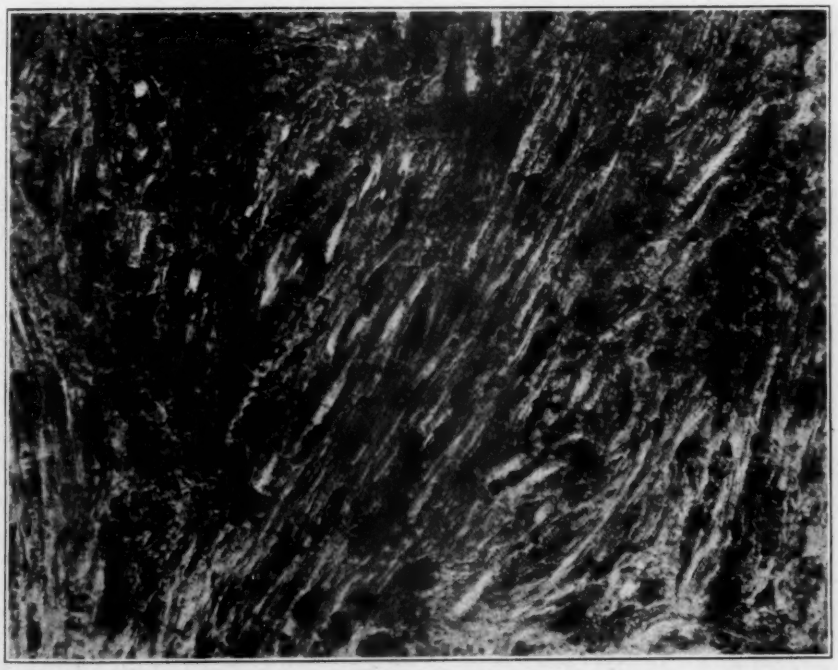

Fig. 6.—Globules and granules arranged in series especially within the fibrils of the connective tissue (intrafibrillar) (sudan IV; × 700).

Sudan IV Stain.—The stratum reticulare at low magnification became brown-red in the region of the altered cutaneous areas (fig. 4). On greater microscopic magnification globules and granules appeared to be arranged in series, especially between and within the fibrils of the connective tissue (figs. 5 and 6). Fat appeared rarely in the cytoplasm. Foam cells could not be demonstrated anywhere. This lipoid was soluble in ether and boiling hot acetone; it was largely, but not completely, soluble in cold acetone and cold or boiling absolute alcohol and insoluble in chloroform.

Nile Blue Sulfate Stain.—Pine-colored globules and granules were present.

Smith-Dietrich Stain.—The fat present was a so-called lipoid and was not neutral fat.

Fischler Stain.—No fatty acids or soaps were present.

Crystal Violet Stain.—Amyloid was not present.

Von Kossa Stain.—Calcium was not formed.

Polarization Microscopic Examination.—Double refractive bodies were not demonstrable.

COMMENT

We have been dealing with 2 patients in whom after trauma (vaccination) and hematogenous infection (rheumatism), respectively, there developed one or more inflammatory nodules in the skin, exhibiting a yellowish color indicative of increased lipoid content. On histologic examination, it was found that predominantly connective tissue was involved. Here two different forms, or perhaps phases, must be distinguished. In some parts of the skin there appeared extraordinary proliferation of connective tissue cells and condensation of the connective tissue fibrils. Between these were cleftlike irregularly limited cavities without a cellular lining and, on being stained with sudan, found to be filled with lipoid. In other words, fat was abundantly deposited in the form of granules and droplets in the fibrillary connective tissue. In other parts the connective tissue cells seemed somewhat diminished in size as compared with the normal; the connective tissue fibrils, on the other hand, were thick and lumpy or even broken off. The pathologic result of the Van Gieson and Weigert stains is a further proof that this connective tissue was diseased. Considering the fact that the collagen had lost its normal affinity for the acid stains and, on the contrary, showed an avid affinity for the basic stains contained in the polychrome methylene blue stain of Unna, the condition must be considered a so-called basophilic degeneration of the collagen.

A remarkable feature was the complete absence of inflammatory cells, of giant cells and, most particularly, of foam cells. As regards the type of fat present, considering the absence of double refraction and the results of the lipoid solubility tests, one may be sure that it was not cholesterol fatty acid ester or free cholesterol. Whereas both of these are completely soluble in hot alcohol and insoluble in boiling acetone, the lipoids in both cases which formed the basis for this report

were completely soluble in boiling acetone and only comparatively, but not completely, soluble in boiling alcohol.

Thus, this lipoid dermatosis is so definitely differentiated clinically, histologically and histochemically that we feel justified in introducing it as a new disease entity with the name imbibitio lipoidica collageni degenerati cutis.

We have still to explain why we consider the condition an imbibition and its classification as a local lipoid disease, in spite of the fact that in both cases reported there appeared a considerable increase in the level of blood cholesterol and in the second case an increase in the total lipids as well (the latter might have been present also in the first case although not manifest in the figures, because the examination was conducted after three weeks of a strictly fat-free diet). The reason for the assumption of a local secondary lipoidosis was that such a lipoid absorption did not occur until years after the appearance of the cutaneous lesions. This fact was proved by the negative lipoid findings in tumors of three years' duration in the first case and further by the absence of lipoid in the cells and its presence only in the fibrillary connective tissue, which presented severe symptoms of degeneration. From these observations, we conclude that the change in the connective tissue was the primary lesion and that lipoid imbibition occurred as a secondary process.

A review of the literature shows that the disease which we have described has apparently been known for several years under other names. Woringer and Kwiatkowski [52] were the first to draw attention to the fact that the cutaneous nodules described by Unna [53] as "fibroma simplex," by Arning and Lewandowsky [54] as "noduli cutanei," by Schreus [55] as "dermatofibroma lenticulare" and by Michelson [56] as "nodular subepidermal fibrosis" possessed the capacity for absorbing fat. Of the opinion that this fat was stored by the histiocytes of the skin, they named it "histiocytoma of the skin." Sézary and Lévy-Coblentz [57] accepted this nomenclature in an article which they published under the characteristic title "From Histiocytoma to Xanthoma," believing that a

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52. Woringer, F., and Kwiatkowski, S. L.: L'histiocytome de la peau, Ann. de dermat. et syph. **3**:998, 1932.

53. Unna, P. G.: The Histopathology of the Diseases of the Skin, translated by N. Walker, New York, Macmillan & Co., 1896, p. 836.

54. Arning, E., and Lewandowsky, F.: Noduli cutanei, eine bisher wenig beobachtete Hautaffektion, Arch. f. Dermat. u. Syph. **110**:3, 1911.

55. Schreus, H. T.: Dermatofibroma lenticulare, Arch. f. Dermat. u. Syph. **161**:456, 1930.

56. Michelson, H. E.: Nodular Subepidermal Fibrosis, Arch. Dermat. & Syph. **27**:812 (May) 1933.

57. Sézary, A., and Lévy-Coblentz, G.: De l'histiocytome au xanthome, Bull. Soc. franç. de dermat. et syph. **40**:798, 1933; Fibrome en pastile et histiocytome, ibid. **40**:1269, 1933.

transition from fat-containing fibromas to xanthomas is possible. Pautrier and Woringer [58] advocated the term histiocytoma for those lesions in which the infiltration with lipoids is relatively slight and the term xanthoma for those in which the cells are supercharged with lipoids, producing cells of the Chambard type. Lewis and Sachs [59] claimed that the lipoidal histiocytomas were fibroxanthomas. The most exhaustive work must be credited to Senear and Caro,[60] who described 25 cases, in some of which there was a definite history of injury to the skin preceding onset of the condition. The lesions varied in size from 1 mm. to 2 cm., were round or ovoid and varied from slightly grayish brown to deep violaceous red, some nodules showing a definitely yellowish hue and peripheral scales. The consistency was of a wooden hardness. Senear and Caro definitely emphasized that they were never able to demonstrate any formation of foam cells but that double refraction could be demonstrated. Because the cells reabsorbed subcutaneously injected saccharated ferric oxide, they considered them to be histiocytes. The authors admitted frankly, however, that the designation "histiocytoma cutis" was open to criticism because one had here to deal not with a true tumor of spontaneous origin but one associated with an inflammatory histiocytosis. Senear and Caro opposed the classification of these tumors in the group of xanthoma, chiefly because no foam cells or Touton's giant cells were demonstrable.

From the clinical description of the lipoid-containing nodules one might conclude that they were identical with those herein described. There exists, however, a fundamental histologic difference. Whereas the authors cited emphasized repeatedly that the lipoid was intracellular, we were able to demonstrate in our cases that the lipoid was exclusively interfibrillary and intrafibrillary. In spite of the fact that we were able to examine four different nodules histologically and that numerous sections were thoroughly studied, we could not demonstrate any lipoid deposition in the histiocytes.

On the basis of our painstaking histologic and chemical examinations we therefore claim that the fibroma-like nodular structures described by Woringer and Kwiatkowski [52] are to be interpreted as xantheloids, whereas in our 2 cases we had to deal with a so-called imbibitio lipoidica collageni degenerati cutis.

Urbach gave the name "xantheloid" to all tumors which have the capacity for storing lipoid substances in their cells. We oppose desig-

58. Pautrier, L. M., and Woringer, F.: L'histiocytome de la peau, Bull. Soc. franç. de dermat. et syph. **40**:1659, 1933.

59. Lewis, G. M., and Sachs, W.: Lipoidal Histiocytoma (Fibroxanthoma): Report of Case, Ann. Int. Med. **9**:1746 (June) 1936.

60. Senear, F. E., and Caro, M. R.: Histiocytoma Cutis, Arch. Dermat. & Syph. **33**:209 (Feb.) 1936.

nations such as xanthofibroma and xanthofibrosarcoma, because they convey the false impression of a combination of fibroma with some other type of tumor.

Although these xantheloids are usually characterized by so-called foam cells and giant cells, Krogius,[61] Garrett [62] and other writers have emphasized the facts that neither the xanthelasma nor the Chambard-Touton giant cells constitute constant features of these tumors and that, on the contrary, the cells of fibroma, sarcoma and granuloma may all store lipoids.

The differential diagnosis must take into consideration, besides Woringer's xantheloids,[52] also a series of other lipoid-containing cutaneous nodules. The lipoid granuloma described by Chester and Kugel [63] in generalized xanthelasmatosis may be distinguished not only clinically but also by its three types of cells, typical foam cells, exudate cells and younger connective tissue cells. Makai's [64] lipoidgranulomatosis subcutanea" consists of subcutaneous nodules in the skin of amputation stumps, which are to be considered as foreign body granuloma. They develop owing to the extrusion of fat from fat cells, due to the constant exposure of the subcutaneous fatty tissue to pressure. The result of this irritation is the aforementioned foreign body granuloma. The sharply defined hard violet-brown plaques of our cases have a certain clinical similarity to the Darier-Roussy sarcoid, certain forms of cutaneous amyloidosis and, particularly, necrobiosis lipoidica. The characteristic histologic picture of the three mentioned dermatoses permits their rapid distinction from the lipoid dermatosis herein presented.

SUMMARY

This study contains a suggested classification for lipoidoses according to clinical, histologic and chemical criteria, an introduction of the concept of "imbibitio lipoidica" in the place of that of "lipoid degeneration" and a presentation of a new local lipoid dermatosis, "imbibitio lipoidica collageni degenerati cutis."

61. Krogius, A.: Zur Kenntnis der sogenannten Xanthosarkome der Sehnenscheiden, Acta chir. Scandinav. **55**:363, 1923.

62. Garrett, C. A.: Tumors of the Xanthoma Type, Arch. Surg. **8**:890 (May) 1924.

63. Chester, W., and Kugel, V. H.: Lipoidgranulomatosis (Type, Hand-Schüller-Christian): Report of Case, Arch. Path. **14**:595 (Nov.) 1932.

64. Makai, E.: Lipogranulomatosis subcutanea am Amputationsstumpf (Prothesenrandknoten), Zentralbl. f. Chir. **57**:590, 1930.

SCLEROSING SOLUTIONS

A PHOTOGRAPHIC METHOD FOR STUDYING THEIR EFFECTS ON TISSUE

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Experimental studies on animals with different sclerosing solutions have been carried out before. Wolf [1] studied histologic alterations following injection of solution of mercury bichloride; Meisen [2] reported histologic changes following the use of sodium salicylate, and Dörffel,[3] changes following the injection of sugar and saline solutions. Similar experimental studies have been made by Regard,[4] Schwarz and Ratschow [5] and others. As a rule the blood vessels of rabbits' ears have been used, and the veins of dogs and horses have also served.

Comparative studies of different solutions applied to the aural veins and the subcutaneous tissue of rabbits were made by Schubert [6] in 1933. He examined and compared the effectiveness of sodium morrhuate solution of 3 to 10 per cent concentration, invert sugar solution of high viscosity and high concentration, hypertonic solution of sodium chloride and alcohol from 70 to 100 per cent. All investigators based their conclusions on the clinical aspect and the histologic observations.

For the past two years the varicose veins clinic of the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital has secured effective results with relative absence of side effects by the use of an invert sugar solution of high viscosity and high concen-

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From the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, Columbia University.

1. Wolf, E.: Die histologischen Veränderungen der Venen nach intravenösen Sublimateinspritzungen, Med. Klin. **16**:800, 1920.

2. Meisen, V.: A Lecture on Injection Treatment of Varicose Veins and Their Sequelae (Eczema and Ulcer Cruris) Clinically and Experimentally, Acta chir. Scandinav. **60**:435, 1926.

3. Dörffel, J.: Experimentelles und Klinisches über Krampfaderverödung, Dermat. Ztschr. **51**:41, 1927.

4. Regard, G. L.: Le traitement des varices par les injections sclérosantes, Rev. méd. de la Suisse Rom. **45**:102, 1925.

5. Schwarz, E., and Ratschow, M.: Experimentelle Untersuchungen über die künstliche Verödung von Venen, Zentralbl. f. Chir. **56**:1474, 1929.

6. Schubert, M.: Experimentelle Untersuchungen über die gefässverödende Wirkung des Natrium morrhuolicum im Vergleich mit den gebräuchlichsten Zucker- und Salzlösungen, Beitr. z. klin. Chir. **157**:55, 1933.

tration.[7] The experiments to be reported were undertaken to find the reason for the results obtained in the clinic.

The rabbit's ear is an excellent test object for comparative examinations. The anatomic relations and the caliber of the blood vessels are about the same in every animal of the same size, with the arterial system in the center of the ear and the veins on the borders connected by communicating blood vessels and all visible when observed against a source of light. Observations on the obliterative process of the blood vessels of the rabbit's ear indicated that the red blood vessels turned yellowish after obliteration, that inflamed areas became red, that insufficient obliteration or recanalization of the blood vessels caused them to appear again, while the obliterated veins and connective vessels once visible disappeared entirely. Accordingly I followed these changes photographically. After a series of experiments it has been found that photographs depicting clearly the course of events could be obtained by photographing the rabbits' ears against a flashlight.

Because of the small caliber and capacity of the vein of the rabbit's ear, amounts of solutions have been used in relative proportion to the amount used and indicated for the treatment of varicose veins, according to the table of McPheeters.[8] In the following tabulations only those solutions used in my experiments are reported on.

Solution	Sodium Morrhuate	Sugar	Quinine and Ethyl Carbamate (Quinine Urethane)	Sodium Chloride
Strength	½ to 10%	50 to 75%	2%	20%
Dose	0.5 to 5 cc.	5 to 30 cc.	0.5 to 2 cc.	5 to 30 cc.

Solution	Sodium Morrhuate	Invert Sugar of Low Viscosity*	Invert Sugar of High Viscosity†	Quinine and Ethyl Carbamate (Quinine Urethane)	Sodium Chloride Sodium Salicylate
Strength	5%	60%	80%	2%	30%
Dose	0.25 to 0.3 cc.	0.5 cc.	0.25 to 0.5 cc.	0.15 to 0.25 cc.	0.3 cc.

* Invert sugar (Lilly) was used in these experiments.
† Levodex (Endo) was used in these experiments.

METHOD

With the technic based on my experience and on that of other authors, I injected the solutions either into the bloodless or into the blood-filled vein, imitating the procedure used in the treatment of varicose veins. Subcutaneous and paravenous injections were also given. Fine hypodermic needles with short points were used. The ears were photographed prior to injection, a few days after the treatment and at the end of the observation period. A lens opening of 22 was used with a no. 21 flash bulb, and the photographs were taken on Defender brand H. G. S. portrait film. The lens was placed 18 to 20 inches (45 to 51 cm.)

7. As an invert sugar of high concentration and high viscosity levodex (Endo) has been used; as an invert sugar of high concentration and low viscosity invert sugar (Lilly) was employed.

8. McPheeters, H. O., and Anderson, J. K.: Injection Treatment of Varicose Veins and Hemorrhoids, Philadelphia, F. A. Davis Company, 1938.

from the ears, which were held still by hand. The flash bulb was held behind and below the ears, so that the light showed through the ears without producing a halation on the photograph. The photographic plate is sensitive for red; therefore, red turns black in the picture (blood vessels and inflamed areas). Obliterated blood vessels become yellowish and are not visible in the photograph. Effective obliteration of the veins in a rabbit's ear is followed by infarct if blood circulation is not restored in due time.

EXPERIMENTS

The experimental data are presented in the accompanying tabulation.

Experiment 1

	After Four Days (Fig. 1A)	After Seven Days	After Ten Days	After Eighteen Days (Fig. 1B)
Left ear: 0.25 cc. sodium morrhuate injected into blood-filled lateral vein	Slight inflammation	Inflammatory reaction decreasing	Almost normal	Normal
Right ear: 0.5 cc. invert sugar of high viscosity injected into bloodless vein and kept there for four minutes	Inflammation	Swelling and inflammation	Slight necrosis	Necrosis of lateral border of ear

Sodium morrhuate, 0.25 cc., injected in the blood-filled vein caused only a slight inflammation and was not effective enough to obliterate the vein. An invert sugar of high viscosity, 0.5 cc., injected in the bloodless vein and left there for four minutes obliterated the vein.

Experiment 2

	After Four Days	After Seven Days	After Ten Days	After Twenty-One Days (Fig. 2)
Left ear: Subcutaneous injection of 0.5 cc. sodium morrhuate. Dime-sized wheal	Inflammation, beginning necrosis	Inflammation and necrosis; cartilage affected	Injection site covered with crust	Scarring; still inflamed; distortion of ear due to damage to cartilage
Right ear: Subcutaneous injection of 0.5 cc. invert sugar of high viscosity. Subcutaneous bleeding in wheal	Hematoma; ear inflamed	Superficial necrosis	Injection site covered with crust	Scarring; still inflamed

Both sodium morrhuate, 0.5 cc., and invert sugar of high viscosity, 0.5 cc., injected subcutaneously caused inflammation and necrosis. The sugar solution affected the skin only, whereas the sodium morrhuate damaged the cartilage.

Experiment 3 (Same Animal)

	After Three Days	After Five Days (Fig. 3A)	After Eight Days	After Ten Days	After Fifteen Days	After Twenty-Four Days (Fig. 3B)
Left ear: 0.3 cc. of a 30% solution of sodium salicylate injected into blood-filled vein *	Inflammation; ear drooping	Severe inflammation	Beginning necrosis	Demarcation of necrosis	Still inflamed; demarcation progressing	Infarct
Right ear: 0.3 cc. of a 30% solution of sodium chloride injected into blood-filled vein	Inflammation	Inflammation	Slight necrosis	Demarcation	Less inflammation; border covered with crusts	Infarct

* Rabbit cried during the injection, perhaps some drops of the solution entered paravenously.

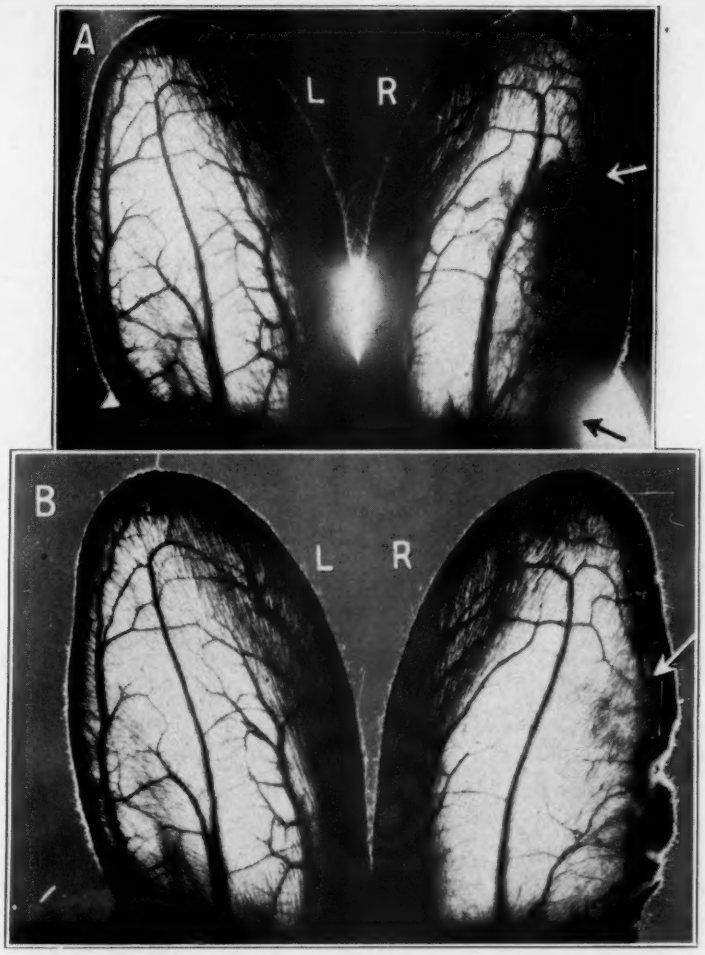

Fig. 1.—*A*, the left ear does not reveal signs of inflammation after injection of 0.25 cc. of sodium morrhuate into the blood-filled vein. On the right ear the severely inflamed area between the arrows is due to 0.5 cc. of an invert sugar of high viscosity, which was injected into the bloodless vein and kept there for four minutes. Halation is present because the flashlight was not held low enough. *B*, the left ear is normal (failure of sodium morrhuate). The right ear shows obliteration of the lateral vein below the injection site (indicated by arrow), causing infarct.

Fig. 2.—Inflammation of both ears resulting from subcutaneous injections: left, 0.5 cc. of sodium morrhuate; right, 0.5 cc. invert sugar of high viscosity. The left ear is disfigured owing to corrosion of the cartilage.

Sodium salicylate and sodium chloride caused obliteration.

Experiment 4

	After Three Days	After Five Days (Fig. 4A)	After Ten Days	After Fifteen Days	After Twenty-Four Days (Fig. 4B)
Left ear: 0.3 cc. sodium morrhuate injected into blood-filled vein	Inflammation; drooping ear	Ear swollen and inflamed	Lateral side of ear swollen and inflamed	Shrinking of border line; inflammation still present	Infarct
Right ear: 0.5 cc. of a 60% solution of invert sugar of low viscosity injected into blood-filled vein	No reaction	.....	.....	.....	Normal

Injection of invert sugar of low viscosity, 0.5 cc. of a 60 per cent solution, into a blood-filled vein was ineffective. Obliteration was caused by 0.3 cc. of sodium morrhuate.

Experiment 5 (Same Animal)

	After Two Days
Right ear: 0.25 cc. of a 2% solution of quinine and ethyl carbamate (quinine urethane) injected into blood-filled vein	No reaction

Failure resulted from use of quinine and ethyl carbamate (quinine urethane), 0.25 cc.

Experiment 6

	After One Day	After Three Days	After Five Days (Fig. 5A)	After Ten Days	After Nineteen Days (Fig. 5B)
Left ear: 0.5 cc. of physiologic solution of sodium chloride injected subcutaneously; wheal	Slight inflammation	Reaction subsided. Levodex, 0.5 cc., injected into blood-filled vein	Inflammation of lateral side of ear	Slight inflammation, with some knots in vein	Disappearance of lower half of vein; no inflammation
Right ear: 0.15 cc. of a 2% solution of quinine and ethyl carbamate (quinine urethane) injected into a blood-filled vein	No reaction	Slight pinhead-sized area of inflammation	Pea-sized area of inflammation	Reaction subsided	

Physiologic solution of sodium chloride, 0.5 cc. subcutaneously, did not affect the tissue. Quinine and ethyl carbamate (quinine urethane), 0.15 cc., injected into a blood-filled vein was a failure. An invert sugar of high viscosity, 0.5 cc., injected into a blood-filled vein obliterated the vein.

Experiment 7 (Same Animal)

	After Ten Minutes	After Two Days (Fig. 6A)	After Six Days	After Fifteen Days	After Nineteen Days (Fig. 6B)
Left ear: 0.25 cc. of a 2% solution of quinine and ethyl carbamate (quinine urethane) injected paravenously	Site of injection bleached	Extensive inflammation and beginning necrosis	Beginning demarcation of necrosis	Dry necrosis	Necrosis of large area
Right ear: 0.25 cc. of invert sugar of high viscosity injected into bloodless vein and kept there for four minutes	Slight inflammation along vein	Inflammation	Inflammation; border of ear covered with crusts	Vein obliterated; slight superficial scarring on internal surface; a little inflammation still visible	Still slight inflammation present; slight scarring; vein obliterated

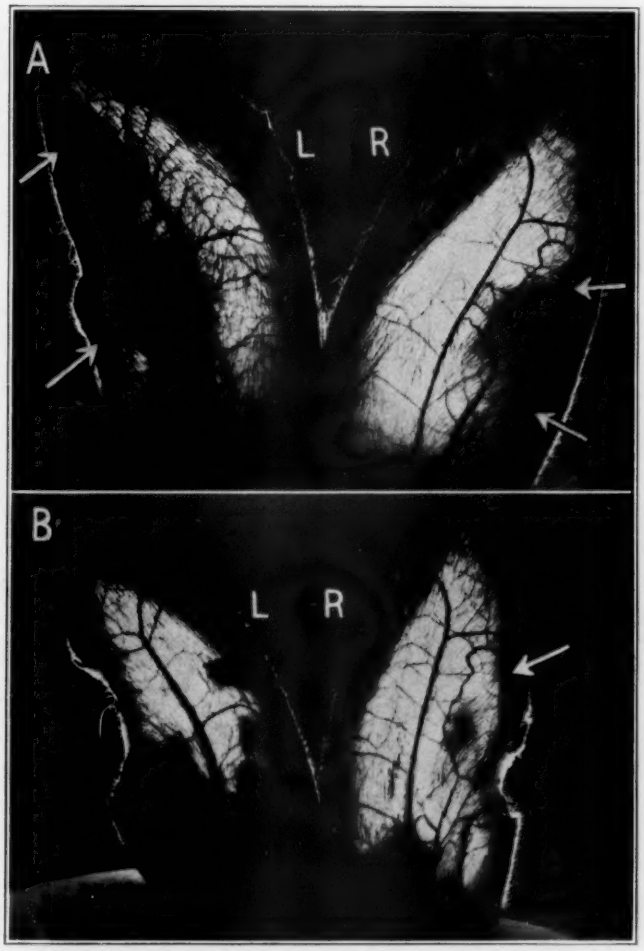

Fig. 3.—*A*, the intensive inflammation of the left ear results from the intravenous and probably accidental paravenous injection of 0.3 cc. of sodium salicylate. The inflammation of the right ear is due to 0.3 cc. of sodium chloride which was injected into the blood-filled vein. *B*, necrosis of the left ear and infarct of the right ear, with obliteration of the lateral vein below the point indicated by the arrow (fig. 2). The inflammatory processes of both ears are injury marks due to the fastening of metal ear tabs by mistake and their later removal.

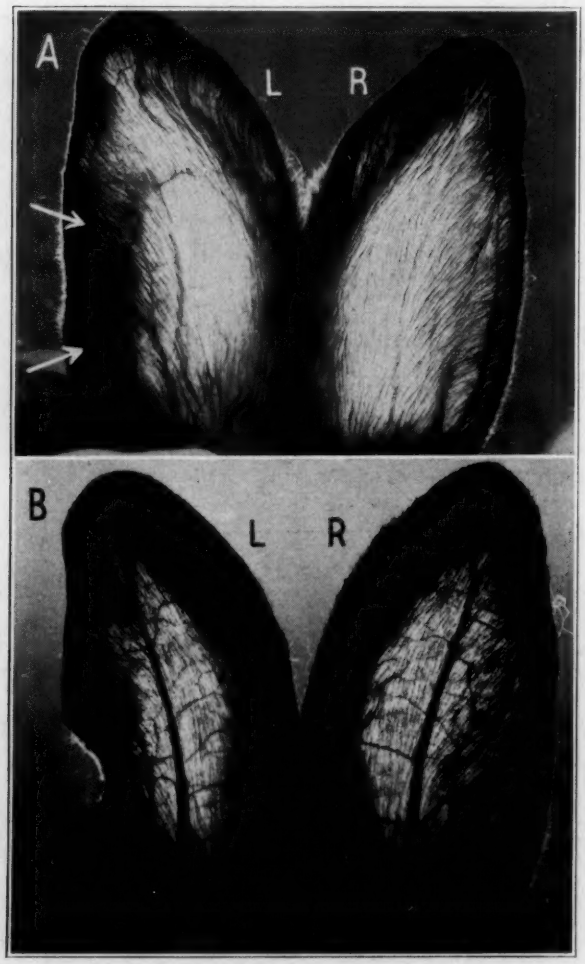

Fig. 4.—*A*, the lateral vein of the left ear is invisible in the inflamed tissue as a result of 0.3 cc. of sodium morrhuate which was injected into the blood-filled vein. The right ear is normal after injection of 0.5 cc. of a 60 per cent solution of invert sugar of low viscosity into the blood-filled vein. The picture is poor. Perhaps the flashlight was held too far from the ears. *B*, infarct of the left ear indicates effectiveness of sodium morrhuate. The normalcy of the right ear vein proves the failure of invert sugar of high concentration and low viscosity.

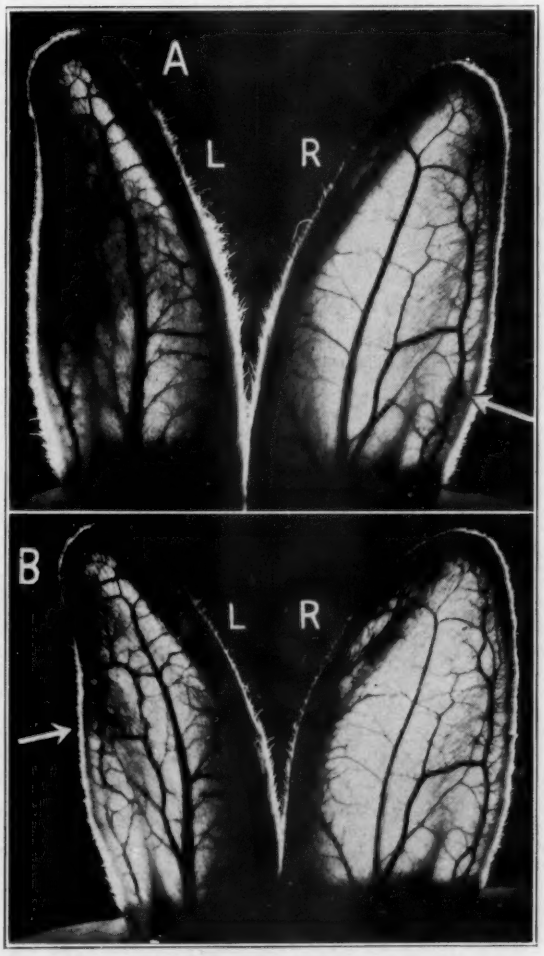

Fig. 5.—*A*, the left ear shows inflammation in the lateral part and haziness of the blood vessels after the injection of 0.5 cc. of invert sugar of high viscosity into the blood-filled vein. On the right ear (arrow) is a pea-sized area of inflammation resulting from 0.15 cc. of quinine and ethyl carbamate (quinine urethane) injected into the blood-filled vein. *B*, the obliteration of the lateral vein of the left ear below the site indicated by the arrow demonstrates the effectiveness of invert sugar of high viscosity; the normalcy of the right ear, the failure of quinine and ethyl carbamate.

Severe necrosis occurred after paravenous injection of 0.25 cc. of quinine and ethyl carbamate (quinine urethane). Obliteration of vein was caused by the injection of 0.25 cc. of invert sugar of high viscosity into bloodless vein.

TABLE 1.—*Summary of Experiments*

Solution	Amount	Administration	Result
Sodium chloride, 30%	0.3 cc.	In blood-filled vein	Obliteration; infarct
Sodium salicylate, 30%	0.3 cc.	In blood-filled vein	Obliteration; infarct
Sodium morrhuate, 5%	0.3 cc.	In blood-filled vein	Obliteration; infarct
Sodium morrhuate, 5%	0.25 cc.	In blood-filled vein	No obliteration
Sodium morrhuage, 5%	0.5 cc.	Subcutaneously	Necrosis of skin and cartilage
Quinine and ethyl carbamate (quinine urethane), 2%	0.15 cc.	In blood-filled vein	No obliteration
Quinine and ethyl carbamate (quinine urethane), 2%	0.25 cc.	In blood-filled vein	No obliteration
Quinine and ethyl carbamate (quinine urethane), 2%	0.25 cc.	Paravenously	Severe necrosis
Physiologic solution of sodium chloride	0.5 cc.	Subcutaneously	No reaction
Invert sugar of low viscosity, 60%	0.5 cc.	In blood-filled vein	No reaction
Invert sugar of high viscosity, 80%	0.5 cc.	In blood-filled vein	Obliteration
Invert sugar of high viscosity, 80%	0.5 cc.	In bloodless vein	Obliteration; infarct
Invert sugar of high viscosity, 80%	0.25 cc.	In bloodless vein	Obliteration only
Invert sugar of high viscosity, 80%	0.5 cc.	Subcutaneously	Necrosis of skin

The experiments and pictures support my clinical observations.[9]

TABLE 2.—*Summary of Clinical Observations*

Solution	Results with Careful Injection	Concomitant Symptoms	Secondary Reactions	Results from Accidental Paravenous Injections
Sodium salicylate or sodium chloride	Excellent	Intensive cramp during and after injection	.....	Intensive paraphlebitis and slough
Invert sugar solution of high concentration and low viscosity	Failure or obliteration with frequent recanalization	.....	.....	Burning pain of short duration
Invert sugar solution of high concentration and high viscosity, with special technic (injection into bloodless vein)	Excellent	Slight cramp of two to three minutes' duration	.....	Burning pain of short duration
Quinine and ethyl carbamate (quinine urethane)	Good or doubtful	.....	Angioneurotic symptoms; quinine allergy	Painful slough
Sodium morrhuate	Excellent, good or doubtful	.....	Allergic reaction (shock, pruritus, dermatitis)	Sometimes slough

Schubert,[6] in summarizing his results, pointed out that sugar solution is the most harmless one; it never causes extensive defects, no matter where it is injected. Hypertonic solutions of sodium chloride are the most destructive, and sodium morrhuate lies between the two extremes.

9. Isaak, L.: High Viscosity Invert Sugar: A New Sugar Solution for a More Efficient Treatment of Varicose Veins, M. Rec. **147**:307, 1938.

COMMENT

The experiments on the aural veins of rabbits were undertaken to test the results observed in the clinic where an invert sugar of high viscosity has been used successfully in the obliterative treatment of

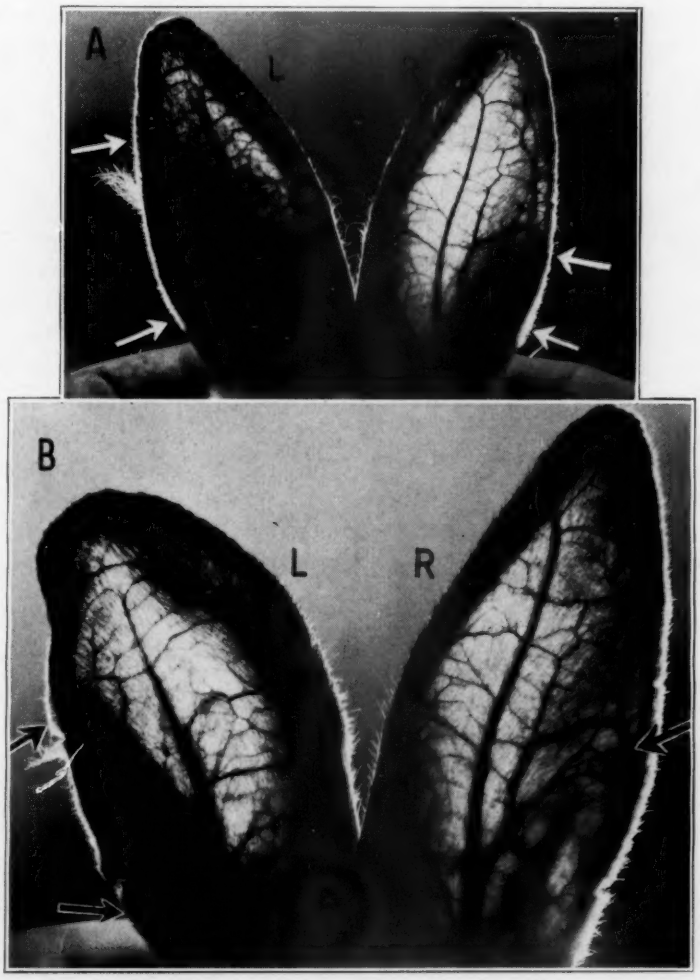

Fig. 6.—*A*, the severe inflammation of the left ear is due to the paravenous injection of 0.25 cc. of quinine and ethyl carbamate (quinine urethane). The slight inflammation of the lower lateral portion of the right ear is a result of 0.25 cc. of invert sugar of high viscosity injected into the bloodless vein. *B*, the dark area on the left ear is dry necrotic tissue, and inflammation is apparent in the demarcated zone. The right ear shows some inflammation in the lower lateral half. Below the arrow the lateral vein is invisible, showing the effectiveness of 0.25 cc. of invert sugar of high viscosity injected into the bloodless vein.

varicose veins. They prove that there is a difference in the obliterative effect of invert sugar solutions of high concentration and low viscosity and of invert sugar solutions of high concentration and high viscosity. They justify the decision to abandon invert sugar solutions of high concentration and low viscosity in favor of a more effective solution, such as that of sodium morrhuate. The experiments on animals manifest that invert sugar of high viscosity is still better and safer than sodium morrhuate in its sclerosing effect. The experiments bear out clinical observations. One has to admit that the technic of the administration of the invert sugar of high viscosity into a bloodless vein is more difficult than that of other solutions, and it is true that fewer patients can be treated in the relatively short clinical hours. I observed, however, that fewer injections of levodex would cure the patients than of sodium morrhuate. Few failures were noticed, and in spite of more prompt results the number of patients receiving treatment for varicose veins increased, perhaps owing to the effective treatment and the lack of by-effects and after-effects.

The experiments on rabbits' ears differ from the treatment of varicose veins in that infarcts are often seen on the treated ear. This is due to the fact that the blood vessels of the rabbit's ear present a system of end arteries and veins. Every blockade of a larger area of blood vessels results in the formation of an infarct. Obliteration without the formation of infarcts takes place only when the blood circulation is restored in due time.

CONCLUSIONS

1. A method is presented which photographically shows vascular changes in rabbits' ears after injection of sclerosing solutions.

2. The minimum amount of a solution necessary to obliterate a vein can be found easily by the rabbit experiment. By multiplication of the amount obtained with a figure varying from 10 to 30 one can calculate the quantity of solution which will be effective in the treatment of varicose veins.

3. The proposed macroscopic photographic method is preferable to the histologic method in examining sclerosing solutions, because it is more readily carried out, is less expensive and permits the observation of the whole obliterative process and the whole area, as compared with the small area of a histologic section.

4. The experiments prove the correctness of the clinical observations that invert sugar solutions of high concentration and viscosity are more effective and less irritating than sodium morrhuate and other commonly used agents.

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LUPUS ERYTHEMATOSUS PROFUNDUS

REPORT OF AN EXAMPLE WITH CLINICAL RESEMBLANCE TO DARIER-ROUSSY SARCOID

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Lupus erythematosus is a systemic disease with variable cutaneous manifestations. When the acute or chronic inflammatory reaction involves primarily the upper layers of the skin, it produces a distinctive aspect. On the other hand, when the point of attack of a chronic process is principally centered in the lower half of the cutis and in the subcutis, the resultant picture is entirely unlike that of the superficial variety, for here the clinical phenomenon simulates the sarcoid of Boeck and that of Darier and Roussy and also erythema induratum.

In the interest of better understanding, chronic lupus erythematosus should be subdivided further into three types according to the point of maximum reaction in the skin, namely, the superficial, the median and the deep. The last two types possess infiltrative qualities which produce tumor-like formations. The first type includes both the localized and the disseminate form, which are well known to all dermatologists; the second simulates, clinically, sarcoid of Boeck, and the last has a definite clinical resemblance to Darier-Roussy sarcoid and to erythema induratum.

A digest of the literature discloses a rather confusing state of affairs as regards the infiltrative forms of lupus erythematosus. Whenever a case of lupus erythematosus resembling Boeck's sarcoid, or vice versa, is presented for discussion without a report of the microscopic observations, the debate rarely terminates harmoniously. Whitehouse [1] summed up the situation when, in commenting on a debate, he aptly remarked, "this is the usual discussion one hears." Weidman [2] was truly confused by the term "transition sarcoid," coined by Stokes for the infiltrated type of lupus erythematosus. Since the histologic aspect of early sarcoid with its banal inflammatory response might prove misleading in differ-

From the Department of Dermatology and Syphilology, Harlem Hospital.

1. Whitehouse, H. H., in discussion on Maloney, E. R.: A Case for Diagnosis (Lupus Erythematosus, Sarcoid or Erythema Perstans?), Arch. Dermat. & Syph. **31**:439 (March) 1935.

2. Weidman, F. D., in discussion on Stokes, J. H.: Transition Sarcoid: Lupus Erythematosus vs. Sarcoid vs. Angiolupoid, Arch. Dermat. & Syph. **32**:694 (Oct.) 1935.

entiation from lupus erythematosus, this situation could not be applied to the case in question, since the eruption had been present for about six months. In the discussion that followed, Stokes agreed with Weidman that the patient had lupus erythematosus. While it might be possible to unite sarcoid and lupus erythematosus on a clinical and etiologic basis, there is no need for coining a new phrase in this instance, because the microscopic picture created by each is distinctive and entirely dissimilar in fully developed conditions. It is not possible to make a diagnosis of the infiltrated type of lupus erythematosus without recourse to the microscope. Furthermore, multiple diagnoses in the same patient frequently lead to error; yet discussers will agree to a diagnosis of lupus erythematosus and sarcoid in the same patient on clinical grounds alone.[3]

Brocq [4] was probably the first to describe the deep form of lupus erythematosus. Years later Kren [5] and Oppenheim [6] presented typical cases of this disease before the Viennese Dermatological Society. Fordyce [7] was one of the pioneer American dermatologists to consider the possible existence of lupus erythematosus profundus. His patient, a woman aged 20, had typical lupus erythematosus superficialis of the face, with multiple subcutaneous nodules on the face and arms. He considered the subcutaneous tumors and the lupus erythematosus superficialis to have the same causation, but since no histologic report was at hand, the discussers classified the subcutaneous nodules with sarcoids of the Darier-Roussy type.

Oliver's [8] patient, a woman aged 35, had a superficial type of lupus erythematosus for three years, involving the scalp, face and arms. Two months prior to presentation deep-seated nodules appeared on the arms and buttocks. A biopsy was not made. In the discussion that followed the presentation, the deep-seated lesions were considered to be erythema induratum. That these nodules were lupus erythematosus profundus seems highly probable.

Caro's [9] patient, a woman aged 35, presented three violaceous red subcutaneous tumors on the left leg. They were of rubbery consistency,

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3. Van Rhee, G.: Lupus Erythematosus and Sarcoid, Arch. Dermat. & Syph. **13**:293 (Feb.) 1926.

4. Brocq, L.: Sur la nature du lupus érythémateux, Rev. gén. de clin. et de thérap. **9**:113 (Feb. 23) 1895.

5. Kren, O.: Lupus erythematosus, Arch. f. Dermat. u. Syph. **112**:391, 1912.

6. Oppenheim, M.: Lupus erythematosus profundus, Arch. f. Dermat. u. Syph. **115**:847, 1913.

7. Fordyce, J. A.: Lupus Erythematosus with Nodular Lesions Suggesting Sarcoid, Arch. Dermat. & Syph. **11**:852 (June) 1925.

8. Oliver, E. L.: Lupus Erythematosus; Sarcoid, Arch. Dermat. & Syph. **12**:150 (July) 1925.

9. Caro, M.: Spiegler-Fendt Sarcoid, Arch. Dermat. & Syph. **22**:1086 (Dec.) 1930.

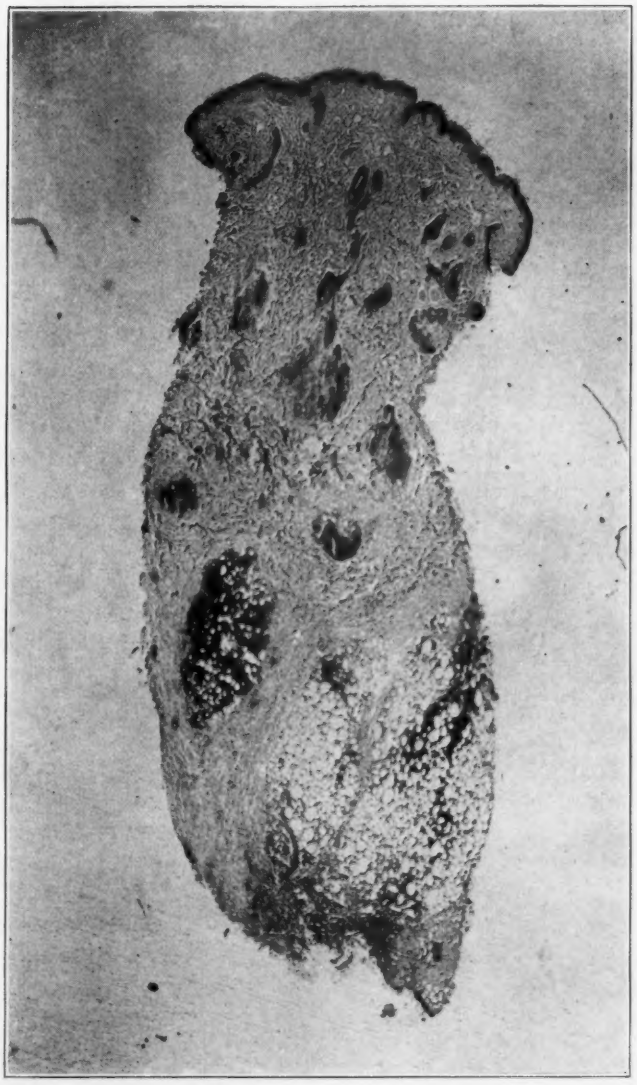

Fig. 1.—Entire section, showing the whole skin involved in the inflammatory reaction.

and they were not attached to the overlying skin. Histologically, the cutis and the subcutis were involved in the inflammatory reaction. The infiltrate consisted of many ill defined groups of cells, composed mainly of lymphocytes, the arrangement of which was perivascular and periglandular. In the deep part of the cutis and in the subcutis the lymphocytes were more numerous and densely packed. Spindle cells were in evidence, and they were more prominent in the deeper portions of the skin. The histologic diagnosis was Spiegler-Fendt sarcoid. This diagnosis was disputed, and the lesions were considered related to the sarcoid of Boeck or of Darier and Roussy. I believe that some of the cases of benign conditions reported under the Spiegler-Fendt classification of sarcoid, including the aforementioned case, are probably instances of lupus erythematosus profundus. The histologic report rendered by Caro certainly favored the deep form of lupus erythematosus.

The case presented by Michelson [10] with a diagnosis of subcutaneous sarcoid was in all likelihood one of lupus erythematosus profundus. A woman aged 43 presented numerous subcutaneous infiltrated plaques on the cheek, arms and hips. They had been present for one year and showed no evidence of ulceration, although atrophy appeared on involution. The infiltrate was diffuse and perivascular and was composed of lymphocytes and polymorphonuclear leukocytes. The sections showed decided "proliferation atrophy." Montgomery [10a] could not correlate the clinical and histologic observations in this particular instance.

Pawlow and Makarjin [11] recounted the clinical and microscopic observations in a patient with lupus erythematosus profundus, which they discussed under the caption "On Tumorous Forms of Lupus Erythematosus." A number of violaceous red subcutaneous tumors had been present on the scalp for four months. The older lesions showed central atrophy. The hair follicles were decidedly dilated and filled with keratotic plugs. The reaction, however, was chiefly observed in the deep part of the cutis and in the subcutis. The perivascular infiltrate consisted almost entirely of lymphocytes. Despite the absence of an associated superficial type of lupus erythematosus, I believe the authors correctly classified the disease.

Without the coexistence of the superficial type, the dermatologist often ignores the diagnosis of the deep form of this disease, despite a

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10. Michelson, H. E.: A Case for Diagnosis (Subcutaneous Sarcoid?), Arch. Dermat. & Syph. **22**:530 (Sept.) 1930.

10a. Montgomery, H., in discussion on Michelson.[10]

11. Pawlow, S. T., and Makarjin, A. A.: Zur Frage von tumorartigen Formen des Lupus erythematodes, Dermat. Ztschr. **59**:111 (Aug.) 1930.

fairly characteristic histologic structure. A report on Stibbens' [12] patient with so-called Darier-Roussy sarcoid is pertinent. A woman aged 33 had movable subcutaneous nodules on the arms and buttocks; some were flesh colored, while others varied from dark red to purple. A nodule excised from the arm showed the reaction located principally in the deep part of the cutis and in the subcutis. The lymphocyte, the chief cell type, appeared in large numbers. The vessels showed evidences of pan-

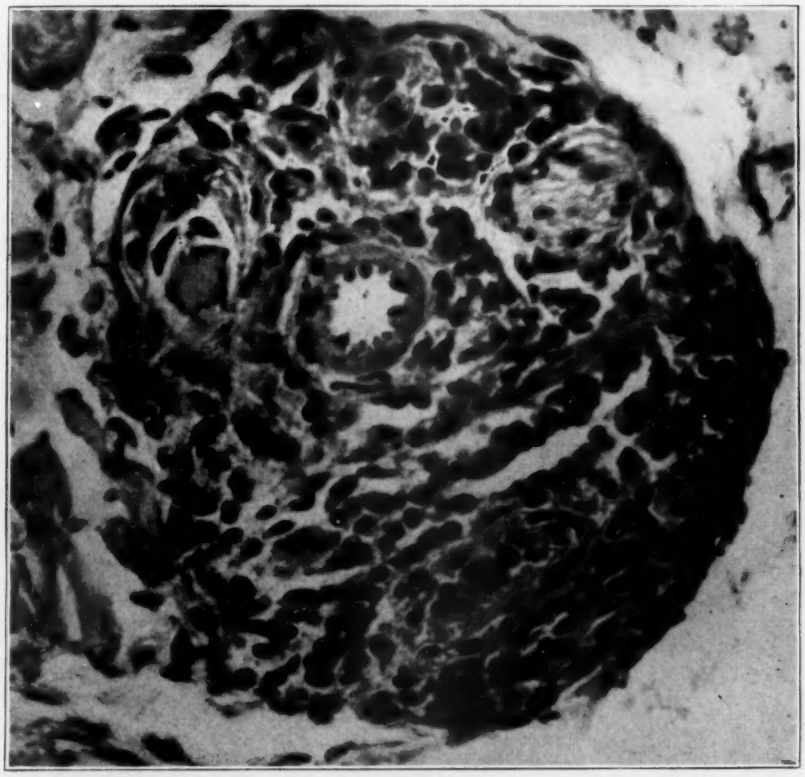

Fig. 2.—The middle third of the cutis, showing morbid changes in a blood vessel (high power). Some of the endothelial cells are undergoing degeneration. The vessel wall is thickened and hyperplastic. Note the perivascular character of the lymphocytic infiltrate. The stroma within this area is undergoing degeneration.

arteritis, and "proliferation atrophy" was present. Epithelioid cells were entirely lacking.

12. Stibbens, F. H.: Multiple Benign Sarcoid (Darier-Roussy Type), Arch. Dermat. & Syph. **24**:1064 (Dec.) 1931.

Fig. 3.—The entire subcutis, with the inflammatory reaction throughout. The cellular reaction is most intense in the upper third.

The appearance of these deep-seated lesions in locations other than the face is disconcerting, and histologic examination is the only recourse for accurate diagnosis. If typical lesions of superficial lupus erythematosus appear practically simultaneously with subcutaneous nodules, it is more than likely that the etiologic factor is the same for both, and there is no necessity for multiple diagnoses in most instances. Comel [13] was

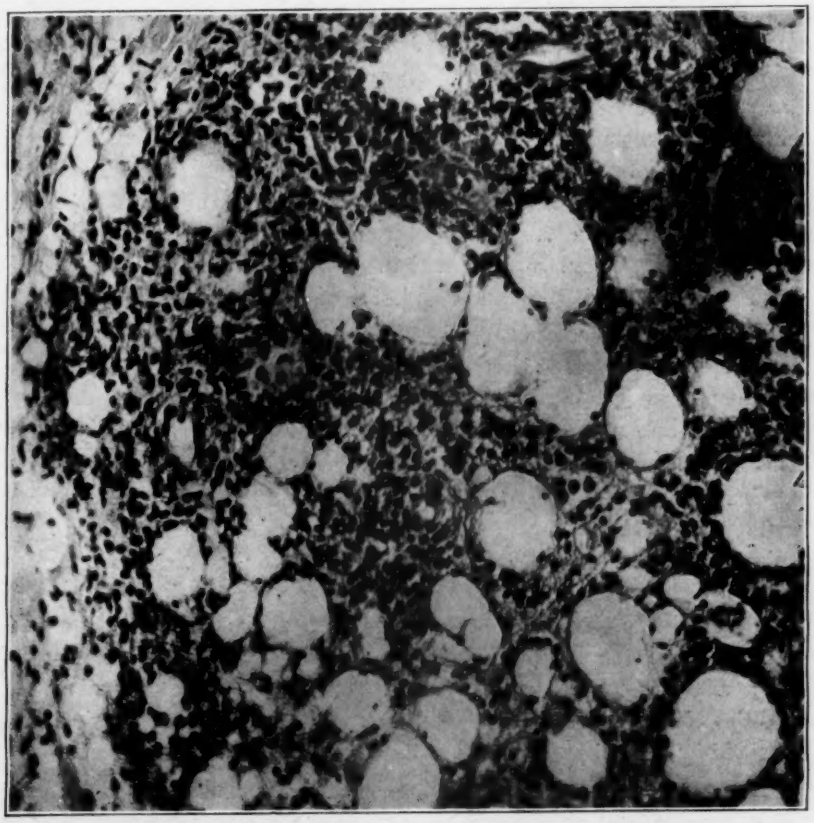

Fig. 4.—A portion of the upper third of the subcutis (high power). The exudate is invading the intercellular spaces and penetrating the fat cells. Some of these cells are distended, and an occasional cell wall shows evidence of rupture. The grouping of a few histiocytes at the left suggests tubercle formation; in no other part of the entire section is this feature encountered.

probably deceived by the presence of infiltrations on the lower extremities when he made a diagnosis of lupus erythematosus tumidus and

13. Comel, M.: Lupus eritematoso tumido associato ad eritema indurato Bazin; contributo al quesito delle microbidi cutanee, Gir. ital. di dermat. e sif. **73**:1812 (Dec.) 1932.

erythema induratum for the same patient, despite the similarity of the histologic structure of the lesions on the face and on the legs. These findings apparently surprised the author, who was unable to find a tuberculoid architecture in either section. Comel's patient, a woman aged 31, had had a tuberculous infection of the cervical lymph nodes for many years. Five years prior to observation small red nodules appeared on the face and on the dorsa of both hands. Two years previously irregular, deep-seated infiltrated plaques developed on the legs. The plaques were dark red to violaceous, and there was a tendency for all lesions to undergo remission and exacerbation, regardless of treatment. Examination revealed scars from a healed tuberculous infection of the cervical lymph glands and an active tuberculous process involving the submaxillary lymph glands. Comel is the authority for the statement that follicular hyperkeratosis is demonstrable only microscopically in patients with lupus erythematosus profundus and that resolution may occur with or without scar formation. He also stated that the microscope reveals edema, congestion and foci of lymphocytic infiltration.

Traub's [14] patient undoubtedly had lupus erythematosus profundus; yet, despite suggestive microscopic evidence, there was no unanimous agreement among the physicians at the presentation. Fraser stated the belief that the eruption was sarcoid, although he stressed the fact that some parts of the section suggested lupus erythematosus.

Chargin and Wolf [15] presented a case with a diagnosis of lupus erythematosus of the face and sarcoid of the arm. In addition to the typical superficial type of lupus erythematosus of the face, subcutaneous nodules were present. These lumpy lesions were similar to those on the arm. In the discussion the nodules on the face and arm were considered to be sarcoid either of the Boeck or of the Spiegler-Fendt type. Later a microscopic examination of sections of nodules from both localities showed identical histologic structures, and the condition was classified by several pathologists as the deep form of lupus erythematosus.

Lupus erythematosus profundus is little recognized as a definite clinical entity, and since there is lack of unanimous agreement among experienced pathologists [16] as to the actual existence of this variant of lupus erythematosus, it was considered opportune to report the following case.

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14. Traub, E. F.: A Case for Diagnosis (Sarcoid? Lupus Erythematosus Profundus?), Arch. Dermat. & Syph. **34**:538 (Sept.) 1936.

15. Chargin, L., and Wolf, C.: Lupus Erythematosus of the Face and Boeck's Sarcoid of the Arms, Arch. Dermat. & Syph. **36**:458 (Aug.) 1937.

16. Satenstein, D. L., in discussion on Chargin, L., and Wolf, C.: Lupus Erythematosus of the Face and Boeck's Sarcoid of the Arms, Arch. Dermat. & Syph. **40**:499 (Sept.) 1939.

REPORT OF CASE

A white married woman aged 23, a native of Puerto Rico, was first seen on Jan. 11, 1939. Since migrating to the United States eight years previously, she had been a resident of New York. Both her uncle and aunt had died from pulmonary tuberculosis in Puerto Rico six years and two years before, respectively. She had measles and mumps during childhood but recovered from these uneventfully.

The patient had been in apparent good health until 1936. At this time, while she was visiting her native land, large masses appeared on both sides of the neck. These superficial, painless tumors, apparently tuberculous lymphadenitis, resisted varied types of treatment but subsided gradually two years later, only to recur in milder form within six months. On admission to the clinic her symptoms were purely objective. She complained of a small mass on the back and an eruption on the face, which had been present for six months and four months, respectively. On the right cheek were four closely aggregated red superficial edematous slightly scaly lesions, varying in size from that of a pinhead to that of a split pea. A single split pea–sized lesion was present on the left cheek. A single flesh-colored well defined smooth subcutaneous flat plaque, about the size of a 50 cent piece, was observed on the upper part of the left side of the back near the shoulder. It was firm and elastic, and its elevation above the surface was barely noticeable. The skin over this mass appeared normal; there were no scales, and dilated follicular orifices were not noted. The tumor was not attached to the skin, and it was freely movable over the deep tissues. No lesions were noted on the buccal mucosa. The anterior cervical lymph glands were slightly enlarged. They were symmetric, discrete, painless, flesh colored and freely movable. The presumptive clinical diagnoses were lupus erythematosus of the face, Darier-Roussy sarcoid of the back and tuberculous lymphadenitis. In addition to the conditions noted, there was a mild hypotension; the systolic blood pressure was 104 and the diastolic 76; otherwise the results of physical examination were normal.

A biopsy was made of the lesion of the back on January 12. An intracutaneous injection of 0.1 cc. of old tuberculin in dilution of 1:100,000 produced a strongly positive reaction, which persisted for about six weeks. The blood Wassermann reaction was reported as negative. The results of a urine examination were likewise negative, and a blood count gave normal results except that there were 44 per cent lymphocytes. A roentgenogram of the lung showed no abnormalities.

The facial lesions showed evidences of resolution four days after the tuberculin test and before the commencement of therapy with a gold compound, which was instituted on February 7. Eight intravenous injections of gold sodium thiosulfate were administered at weekly intervals; the initial dose was 25 mg., and the others were 50 mg. except the last, which was reduced to 10 mg. because of a beginning palmar keratosis. A generalized gold dermatitis appeared four days after the last treatment, that is, on April 4. It was a symmetric, intensely pruritic erythematopapular eruption. This complication resolved rather slowly with sodium thiosulfate therapy, and during the process of involution the dermatitis assumed a pityriasis-rosea-like appearance. An examination of the blood performed on May 10 showed slight secondary anemia and mild leukopenia (4,600 leukocytes per cubic millimeter), with a normal white cell differential count. On May 23 the lupus erythematosus of the face was not in evidence. The gold dermatitis having likewise completely disappeared, the patient was given weekly intramuscular

injections of bismuth subsalicylate; the initial dose was 1 cc., but later the dose was increased to 1.5 cc. of the suspension. On July 7, or five months after the institution of aurotherapy, the subcutaneous tumor of the back and the palpable cervical lymph glands had completely disappeared. Healing of the former lesion resulted in slight atrophy. During treatment with both gold and bismuth preparations, the patient received intracutaneous injections of old tuberculin at intervals of three to four weeks. Dilutions were increased rapidly to determine the degree of sensitivity. Hyperergy to tuberculoprotein was present, since a positive reaction resulted from an injection of 0.1 cc. of a 1 to 1,000,000,000,000,000 dilution.

The inflammation involved the entire skin. The stratum corneum appeared normal except in localities where it effectively plugged an occasional dilated follicular or sweat duct orifice. These localized hyperkeratoses were difficult to detect and were seen only after a number of sections were examined. Parakeratosis was absent. The epidermis was narrowed for the most part. Epidermal atrophy involved chiefly the suprapapillary rete; a few normal rete pegs were seen, but in the majority of instances they were either decidedly diminished in size or completely effaced. Areas of vacuolation were noted throughout the various layers of the epidermis. Liquefaction necrosis of the basal layer was not in evidence. The keratohyaline layer was entirely lacking in small isolated parts of the section, but in the main it was represented by a single row of cells, a number of which were in the process of vacuolar degeneration.

Edema was noticeable everywhere in the cutis and subcutis. It was both interstitial and parenchymatous. In the upper fourth of the cutis the edema was diffuse, while in the deeper portions of this area it was limited, surrounding and permeating the zones of infiltration. The collagenous fibers were widely separated and distended by the serous exudate. In the subcutis fibrinous exudate was widespread and intense. It not only separated the fat cells but also penetrated the wall of an occasional cell, with resultant distention and even rupture.

The lymph vessels of the papillary and subpapillary zones were greatly distended, in contrast to the capillaries, which were only slightly expanded. In the subcutis, however, ectasia of the latter vessels was much greater.

The compact cellular infiltration, periglandular and perivascular, was particularly intense in the lower half of the cutis and throughout the subcutis. It was well defined in the cutis but diffuse in the subcutaneous tissues. The infiltrate was composed mainly of small lymphocytes. Small to moderate numbers of histiocytes and plasma cells were likewise observed. In some foci of the lower part of the cutis, this compactness of the infiltrate was lost because of the edema within these areas; the appendages within these zones were invaded and almost completely destroyed. Within the limits of the infiltrate the collagenous fibers were in a state of degeneration. Fragmentation was especially noticeable in zones where the edema was most intense. Necrosis was absent. A decided connective tissue reaction enveloped a single nodule of infiltrate in an outlying area in the lower part of the cutis. A single blood vessel in the midcutis and another in the lower third of this area showed abnormal changes. Some of the endothelial cells were either in a state of degeneration or were completely destroyed. The vessel walls were thickened and hyperplastic. Special staining failed to show acid-fast bacilli.

COMMENT

My observations coincide with those of Comel,[13] who stated that plugging of the dilated orifices of the dermal appendages is evident only microscopically in the deep infiltrated variety of lupus erythema-

tosus. Involvement of the subcutis in lupus erythematosus is admittedly rare. The decided edema and the cellular invasion account for the presence of the deep-seated tumors, which may be flesh colored, reddish or violaceous, depending on the degree of capillary reaction.

The fact that complete resolution resulted during gold, bismuth and tuberculin therapy favors the diagnosis as presented. My patient unquestionably had a tuberculous infection, which was probably contracted during adolescence. The cervical adenitis more than likely resulted from activity of the tubercle bacillus, and the hyperergy to tuberculoprotein is significant. A positive reaction to a dilution of 1 to 1,000,000,000,000,000 is rare in patients with lupus erythematosus. The fact that the superficial facial lesions showed signs of resolution four days after the first intracutaneous injection of tuberculin favors the hypothesis of a tuberculous cause in this instance.

There is no unanimity of opinion regarding the cause of lupus erythematosus. Jadassohn,[17] Goeckerman,[18] Keil,[19] Macleod [20] have stated that they do not believe that the incidence of tuberculosis with lupus erythematosus is any greater than with other dermatoses and that they doubt that the tubercle bacillus is a causative factor in the production of this disease. On the other hand, Bloch and Fuchs [21] were capable of inducing active tuberculosis in guinea pigs by injection of emulsified tissue from areas of lupus erythematosus. Cannon and Ornstein [22] confirmed these observations in 5 of 23 instances. They [23] also observed that subjects with lupus erythematosus were hypersensitive to tuberculin, and this feature was especially great in those who reacted favorably to tuberculin therapy. Highman, Stokes and Pollitzer [24] considered tuberculosis a factor in the causation of this disease.

It is not within the scope of this paper to discuss in detail the pros and cons regarding the relation between tuberculous infection and lupus

17. Jadassohn, J.: Lupus Erythematosus, in Mrăcek, F.: Handbuch der Hautkrankheiten, Vienna, A. Hölder, 1904, vol. 3, p. 298.

18. Goeckerman, W. H.: Is Lupus Erythematosus Discoides Chronicus Due to Tuberculosis? Arch. Dermat. & Syph. **3**:788 (June) 1921.

19. Keil, H.: Relationship Between Lupus Erythematosus and Tuberculosis: Critical Review Based on Observations at Necropsy, Arch. Dermat. & Syph. **28**: 765 (Dec.) 1933.

20. Macleod, J. M. H.: Lupus Erythematosus: Some Observations on Its Etiology, Arch. Dermat. & Syph. **9**:1 (Jan.) 1924.

21. Bloch, B., and Fuchs, H.: Ueber die Beziehungen des chronischen Lupus erythematodes zur Tuberkulose, Arch. f. Dermat. u. Syph. **116**:722, 1913.

22. Cannon, A. B., and Ornstein, G. C.: The Tubercle Bacillus as an Etiologic Factor in Lupus Erythematosus, Arch. Dermat. & Syph. **12**:691 (Nov.) 1925.

23. Cannon, A. B., and Ornstein, G. C.: Lupus Erythematosus: Treatment with Tuberculin, Arch. Dermat. & Syph. **16**:8 (July) 1927.

24. Highman, W. J.; Stokes, J. H., and Pollitzer, S., in discussion on Macleod.[20]

erythematosus. Suffice it to say that in the case presented there was a tuberculous infection which was considered the inciting factor in the production of the cutaneous lesions.

SUMMARY

Chronic lupus erythematosus should be subdivided further into three types: (*a*) superficial, (*b*) median and (*c*) deep. The latter two are definite clinical entities.

Heretofore, lesions of lupus erythematosus profundus have been mistaken for Darier-Roussy sarcoid, Spiegler-Fendt sarcoid and erythema induratum.

Lupus erythematosus profundus should be suspected whenever deep-seated tumor-like lesions are associated with the superficial form. A definite diagnosis can be made only by histologic examination; the microscopic picture is fairly characteristic. Keratotic plugging of the follicular and sweat duct orifices can be observed only microscopically, but serial sections may be necessary to show it.

A case of lupus erythematosus profundus is described. Hyperergy to tuberculin was demonstrated. The lesion resolved during treatment with gold and bismuth preparations and with tuberculin. The tubercle bacillus was probably the inciting factor.

160 Riverside Drive.

LXXXIX.—A HISTOCHEMICAL STUDY OF NEURODERMATITIS

PRELIMINARY REPORT: MICROINCINERATION AND SPECTROGRAPHIC ANALYSIS

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Chronic disseminated neurodermatitis is generally admitted by most dermatologic writers to be a definite clinical entity. The cause is unknown. It is labeled by some "atopic dermatitis," implying that the disease is allergic in nature. However, the mechanism of the production of this disease is still unknown, even if an allergic causation is assumed, since allergy itself is not entirely understood. From a therapeutic standpoint, neurodermatitis is peculiarly resistant even to an allergic regimen that usually produces results in such allergic diseases as hay fever and asthma. It seemed to us, therefore, that an entirely different approach to the study of this disease might be indicated.

Little is known about the mineral content of the skin, either in health or in disease. Electrolytes certainly play a part in the phenomena of osmosis and of surface tension. These and other powerful interacting physical forces probably enter into the production of the various phases of inflammation. The permeability of the capillaries of the skin and of the epithelial cell membrane itself may be greatly influenced by the quality and quantity of the minerals in the cell and in its environment. A study of the mineral content of the skin was therefore undertaken to determine if possible whether skin in patients with neurodermatitis differed in this respect from normal skin or from that of patients with other chronic inflammatory cutaneous diseases.

METHOD

Specimens of healthy and of diseased human skin were studied by microincineration, according to the procedure of Scott, and by a method of spectrographic analysis, described by McMillen and Scott in 1937 and since improved by Scott. By a judicious blending of the study of ashed sections of a tissue with that of its spectrograms, one can obtain a qualitative and relatively accurate quantitative estimate of its minerals in their topographic arrangement.

Studies, observations and reports from the Department of Dermatology of the Barnard Free Skin and Cancer Hospital and the Anatomical Laboratory of Washington University School of Medicine.

Since there are no published reports dealing with normal human skin studied in this way, we first undertook to establish a normal base line estimate of the minerals by a study of 63 biopsy specimens of skin taken from normal persons varying in age from a few weeks to 91 years. Using the same technical procedure, we studied 24 cases of disseminated neurodermatitis. Biopsy specimens from chronically inflamed and from unaffected skin of patients with neurodermatitis were obtained. As a further control, the skin of patients with several other inflammatory cutaneous diseases was similarly studied.

Half of each specimen was prepared for microincineration, while the other half was dissolved in triply distilled nitric acid for spectrographic analysis. Spectrums of skin of patients with neurodermatitis and of normal skin of patients of comparable ages were photographed on the same plate, and all plates were developed under as nearly identical conditions as possible. The relative intensities of the lines of radiation of some of the specimens were measured microphotometrically by Mr. O. J. Baltzer, of the physics department of Washington University.

MICROINCINERATION

In normal human skin of patients in the age group under consideration (3 years to 35) the epidermis contains a relatively large amount of the white ash of calcium and magnesium. The ashed residue of these elements in the epidermis is usually condensed around the nuclear membranes, although in the basal cells the whole cytoplasm is loaded with it. Most of the iron is contained in the cytoplasm. Few if any of the epidermal cells (of skin at this age) lack the white ash of calcium and magnesium, although the outermost cells of the spinous layer are often devoid of the residue of iron.

The epidermal cells of the skin of patients with neurodermatitis contain little of the white ash of calcium and magnesium. In active lesions even the basal cells have lost their white ash. The basal cells of unaffected skin of patients with neurodermatitis retain the white ash in amounts which appear to be normal, while the spinous cells immediately distal to them leave little of this ash after incineration. The residue of iron is located mostly in the nuclei of the spinous cells and in conspicuously larger amounts than in normal nuclei.

In other diseases, such as lichen planus and contact dermatitis, the epidermis is heavily laden with the white ash of calcium and magnesium. In those cases in which an increase of iron is noticeable, the iron oxide is found in the cytoplasm rather than in the nuclei, as in neurodermatitis. We have studied lichen planus, chronic dermatitis, contact dermatitis, senile dermatitis, exfoliative dermatitis, xeroderma pigmentosum, psoriasis and pemphigus. In all these diseases there is a decided increase in the amount of white ash of calcium and magnesium in the epidermis, but only in exfoliative dermatitis and in psoriasis is there a consistent increase in the residue of iron.

SPECTROGRAPHIC ANALYSIS

The microphotometric measurements of the relative intensities of the lines of radiation on the spectrograms of the specimens of skin studied show that the lines for calcium and zinc are of approximately the same intensity in the skin of patients with neurodermatitis and in normal and pathologic control specimens. Those for copper appear in general to be slightly less intense in the skin of patients with neurodermatitis than in either group of control specimens, but in several cases are somewhat more intense. The iron and phosphorus lines are distinctly more intense in the control specimens.

The greatest difference is in the magnesium lines. These are uniformly of less intensity in specimens of both diseased and unaffected skin of patients with neurodermatitis. There is great reduction in the magnesium content of the entire skin of patients with neurodermatitis.

SUMMARY

We wish in this preliminary report to call attention to the consistent variation in mineral content and topographic distribution peculiar to the entire skin of patients with neurodermatitis, as compared with skin both from normal subjects and from patients with a variety of other cutaneous diseases. This variation is so great in the case of magnesium that we believe there is a magnesium deficiency in the skin of patients with disseminated neurodermatitis.

THE SKIN AND CANCER UNIT OF THE NEW YORK POST-GRADUATE MEDICAL SCHOOL AND HOSPITAL, COLUMBIA UNIVERSITY

A HISTORICAL REVIEW

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The signing on Aug. 30, 1934 of articles of agreement and affiliation between the New York Post-Graduate Medical School and Hospital, Columbia University, and the Stuyvesant Square Hospital (formerly the New York Skin and Cancer Hospital) marked an event of importance in American dermatology. The merger was a logical one, as the New York Post-Graduate Medical School and Hospital, one of the oldest graduate schools in the country, and the New York Skin and Cancer Hospital, since its inception the largest dermatologic clinic in America, frequently indulged in the interchange of clinicians and teachers even in their early years. As early as 1885 Dr. George Henry Fox held classes at the New York Post-Graduate Medical School and Hospital for several years before receiving an appointment as professor; and during that time he was an attending physician at the New York Skin and Cancer Hospital and was teaching at the College of Physicians and Surgeons. Others, like Drs. George T. Elliot, George T. Jackson, A. Schuyler Clark and Henry H. Whitehouse, also served both institutions at the same time. There never existed between the two anything but the best of relations; it could not well be otherwise, as their aims were somewhat different. The New York Post-Graduate Medical School and Hospital naturally placed its teaching first, while the New York Skin and Cancer Hospital devoted most of its time to clinical work. Both institutions were organized the same year, 1882.

THE STUYVESANT SQUARE HOSPITAL (FORMERLY THE NEW YORK SKIN AND CANCER HOSPITAL)

On April 8, 1882, the first institution in America devoted entirely to the care of cutaneous diseases and cancer first saw the light of day. On that memorable occasion a number of distinguished laymen, under the leadership of Dr. L. Duncan Bulkley, gathered in a lawyer's office and associated themselves to form a society with the following objects in view: (1) the treatment of diseases of the skin and cancer by all

known medical and surgical methods; (2) the study of the etiology and pathology of cancer; (3) the study of cancer with a view to its medical treatment, and (4) the reception and care of patients with chronic cancer.

This society was to be known as the New York Skin and Cancer Hospital. The certificate of incorporation was filed on Nov. 11, 1882, and on Jan. 1, 1883, a small private house, at 243 East Thirty-Fourth Street, was purchased for use as a dispensary and hospital for cutaneous diseases and cancer. The lower floor of this building was occupied on January 11 as a dispensary. On February 24 a small back room on the first floor was opened as a ward, with five beds. The first ward patient was admitted on February 26. The upper floors were used for hospital purposes beginning June 2, and on that date twenty-nine beds were installed.

In that first year 774 patients were treated, and in that number were included 49 with cancer. The expense for the first year, ending Sept. 30, 1883, amounted to $13,285.23. The receipts topped this by the large sum of $41.38. Despite this strenuous financial launching, the hospital in its third year owned properties estimated at $80,000; on its fiftieth anniversary in 1932 it had treated approximately 468,189 sufferers from cutaneous disease and cancer, and for the last five years of its existence it had treated a yearly average of 27,847 patients. By 1907, its twenty-fifth year of service, the hospital had treated 62,652 persons, who had made 281,883 visits. In the wards 7,000 patients had spent 311,309 hospital days. These figures are quoted, not in a spirit of vainglory, but simply to convey an idea of the vast amount of clinical work done.

An outstanding member of the group which founded the hospital and the one most responsible for its existence was Dr. L. Duncan Bulkley, as it was he who conceived the original idea. Dr. Bulkley was born in 1845. His father, Henry Daggett Bulkley, gave the first lectures on dermatology in America, at the old Broom Street Infirmary for Diseases of the Skin, as early as 1837. Henry Daggett Bulkley was also president of the New York Academy of Medicine and the New York County and State Medical Societies. It was at his home, 42 East Twenty-Second Street, that the New York Dermatological Society was founded on May 18, 1869. He died in 1872.

His son, L. Duncan Bulkley, studied at the Hôpital St. Louis, after his graduation from the College of Physicians and Surgeons in 1869. On his return to New York he became most active in dermatology. He won the Alvarenga prize in 1891 from the College of Physicians of Philadelphia, with his monograph "Syphilis in the Innocent." He wrote several hundred articles and six or eight textbooks, mostly devoted to dermatotherapy, in which he had a deep interest. He was

one of the founders of the American Dermatological Association, which was formed in Philadelphia on Sept. 6, 1876, at the University of Pennsylvania, and he was the secretary of its first annual meeting, which was held in Niagara Falls, N. Y., on Sept. 4, 1877.

Dr. J. Francis Aitken was the hospital's first house physician, serving from Dec. 1, 1883 to Dec. 1, 1884. He joined the medical staff immediately on the completion of his internship and served continuously until his death, on Aug. 3, 1930. For forty-four years he attended the hospital three days a week. During the twenty years that I served with him he never failed to be present the minute the clinic was opened; he rarely if ever missed a day, despite bad weather and no matter how badly he might have felt at times. Dr. Aitken was a master clinician and an expert in "sight diagnosis." He always remained free from hospital politics, and when he did take sides it was always for the oppressed one. He had a great and kindly heart; he loved life, his specialty and his fellowmen.

Dr. George Henry Fox served the hospital from 1883 to 1913 and also gave it of his best, which is no faint praise to any one fortunate enough to have known Dr. Fox and his splendid career, which began seventy years ago. In that interval Dr. Fox received every possible dermatologic honor, the enumeration of which would in itself make a long article. There is no question that the successful passage of the difficult early years of the hospital was due in large part to the devotion and self sacrifice of Drs. Fox, Bulkley and Aitken.

Other medical officers of the hospital in its first year were Drs. Daniel Lewis, W. T. Alexander, Robert F. Weir and Edward L. Keyes. Among the consultants were such famous men as Drs. W. H. Draper, Fordyce Barker, T. Gaillard Thomas, E. G. Janeway, Alfred L. Loomis and Abraham Jacobi.

In 1886 a country branch at Fordham Heights, near High Bridge, was opened for the patients with cancer, in order to give them the benefit of life in the country. Besides the main house there were a number of separate cottage pavilions. The city hospital at 243 East Thirty-Fourth Street was retained as a dispensary and hospital for cutaneous diseases. Its fame increased with the years, and by 1896 the usefulness of the hospital had long outgrown its building. New quarters were therefore imperative, and its board of governors decided to build, on Second Avenue and Nineteenth Street, a structure which would amply hold the increased attendance. This new building (the present location) was erected in 1897 and occupied in 1898.

In the hospital's first year at the new site 1,788 patients were treated in the dispensary and 205 patients in the wards. Little did the men responsible for its career then realize that thirty-three years later in the same building 29,597 people would apply for relief in its dispensary alone.

In 1890 Dr. Henry H. Whitehouse joined the medical staff and served the hospital faithfully for the ensuing thirty-nine years. Next to Dr. J. F. Aitken, he has had the honor of having served longer than any one else on the staff. He was an office associate of Dr. L. Duncan Bulkley for many years. Dr. Whitehouse also served as president of the medical board and was untiring in his service. He was on the consulting staff of the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital at the time of his death on Aug. 24, 1938.

As the years have passed, many of the well known dermatologists, some of whom have since gained well deserved fame, have served the hospital at various times. Among those may be mentioned Dr. George T. Elliot, professor of dermatology at Cornell for many years; Dr. George T. Jackson, who later occupied the chair of dermatology at the College of Physicians and Surgeons; Dr. Howard Fox, professor emeritus of dermatology and syphilology at the New York University College of Medicine; Dr. William B. Trimble, who preceded Dr. Fox in the chair of dermatology at Bellevue Hospital Medical College; Dr. Udo J. Wile, professor of dermatology and syphilology at the University of Michigan; Dr. Edward P. McGavock, professor of dermatology at the Medical College of Virginia for many years; Dr. Fred Wise, professor of clinical dermatology and syphilology at the New York Post-Graduate Medical School and Hospital, and Dr. A. Schuyler Clark, who served the hospital from 1905 to his sudden and untimely death on March 22, 1929. Among the surgeons were such well known men as Daniel Lewis, Willy Meyer, Franz F. Torek, William Seaman Bainbridge and George Semken.

THE NEW YORK POST-GRADUATE MEDICAL SCHOOL AND HOSPITAL

The establishment of postgraduate instruction in medicine in New York is an interesting subject. In 1809 the New York Hospital threw open its wards to both medical students and graduates in medicine. In 1822 the New York Eye and Ear Infirmary and in 1853 the New York Ophthalmic Hospital did the same thing, but it was not until 1877 that the New York Eye and Ear Infirmary definitely stipulated that all its students must present the degree of Doctor of Medicine.

The embryonic life of the New York Post-Graduate Medical School and Hospital began seven years before its birth, which occurred on Nov. 6, 1882. Those responsible for this prenatal life were: Drs. W. A. Hammond, James L. Little, D. B. St. John Roosa, Fred R. Sturgis, M. R. Patten, W. S. Gourley and that great dermatologic pioneer, Henry G. Piffard. These physicians conceived the idea of post-graduate instruction in New York as early as 1875, for in that year they

formed a postgraduate faculty at the New York University Medical College, and they were permitted to grant certificates to physicians completing the course. Their success was so great that by 1881 they realized the inadequacies of the conditions under which they were working and the necessity of a separate building and complete segregation from the undergraduates. The University was not prepared to accede to these just demands, so on April 4, 1882, this group resigned, as Roosa stated at the time, "Like Abraham we did not know the country to which we were going, but the Lord had ordered it and we went." Unsuccessful overtures were made to Cornell and even to Princeton. Frequent meetings were held during the summer and fall of that year. At a meeting on June 27 a committee of organization was formed with Dr. Hammond as chairman, Dr. Sturgis as a member and Dr. Satterthwaite as secretary.

The school opened on Nov. 6, 1882, at the College of Pharmacy on East Twenty-Third Street. One hundred students matriculated in its first year. The faculty consisted of nine professors, eight associate professors and eight instructors. The school grew so rapidly that by its fourth year commodious quarters were secured at 226 East Twentieth Street, and all the rooms above the second floor were devoted to hospital use. Much of this success was due to the unremitting efforts of Dr. D. B. St. John Roosa, one of the outstanding figures in American medicine. Roosa was born in Bethel, N. Y., on Sept. 4, 1838. His college education was acquired at Yale University, and he received the degree of Doctor of Medicine from New York University in 1860. He immediately volunteered his services in the Civil War and as an assistant surgeon served his country faithfully until the end of hostilities. He then spent a year in Vienna in postgraduate work. On his return to New York he gained early recognition as a specialist in diseases of the eye and ear. He became professor of ophthalmology and otology in the medical department of New York University in 1875 and wrote some excellent treatises on his specialty, but apparently one of his great interests in life was the New York Post-Graduate Medical School and Hospital. He was one of its founders, its first professor and its first president, from its beginning in 1882 to his death on March 8, 1908.

The greatest difficulty in the early years of the school was naturally a financial one. Its circumstances were so straitened that its first faculty contributed $50 each to meet its first expense. However, their vision was keen, for in May 1894 a six story building on Second Avenue and Twentieth Street was occupied, and on Jan. 11, 1912 the present twelve story building was erected. In 1924 the United Hebrew Charities Building at Twenty-First Street and Second Avenue was purchased and renamed the James F. McKernon Building in honor of the president of the school. The New York Post-Graduate Medical School and Hospital and the New York Skin and Cancer Unit now occupy the

entire front on Second Avenue between Nineteenth and Twenty-First streets, with much adjacent property on the side streets.

The department of dermatology and syphilology of the New York Post-Graduate Medical School and Hospital at its inception was a part of the department of genitourinary and venereal diseases, under the leadership of Dr. Frederick R. Sturgis, and it was established at the same time as the school. As Dr. Sturgis' time was completely taken up with the teaching of genitourinary diseases, it is logical to suppose that Dr. Henry G. Piffard took up the teaching of cutaneous diseases; this supposition is further strengthened by the fact that he was a member of the original postgraduate faculty at New York University in 1875 and an active leader in the secession of this faculty from the University in 1882. He was on the first list of professors of the New York Post-Graduate Medical School when it was founded on Nov. 6, 1882, and as far as I can ascertain, Piffard limited his work entirely to dermatology. Among his many activities besides teaching was the publication in 1868 of an excellent translation of Hardy's "The Dartrous Diathesis or Eczema and Allied Affections." In 1876 he published his well known "Elementary Treatise on Diseases of the Skin." It was the second textbook on cutaneous medicine to be published in America and was by no means "elementary," as the modest title suggests, but on the contrary was a masterly presentation of the dermatologic knowldege of that day, interspersed by Piffard's practical knowledge of the subject. In 1881 "A Treatise on the Materia Medica and Therapeutics of the Skin" appeared. Piffard was one of the founders of the New York Dermatological Society in 1869 and was present at the organization of the American Dermatological Association on Sept. 6, 1876. Piffard was intensely human and had a brilliant mind and a warm heart. One of my most pleasant recollections was my long and friendly association with Dr. George Henry Fox. After lunch or dinner cigars were lighted, and Dr. Fox's anecdotes of his friend Piffard were a joy to hear. As they were intimates until Piffard's death on June 8, 1910, the stories were many and varied.

It is interesting to note that as early as 1889 the New York Post-Graduate Medical School and Hospital recognized the advisability of full time instruction in dermatology and its separation from genitourinary diseases. A separate dermatologic department was at long last organized, with George Henry Fox as professor, G. T. Jackson and F. B. Carpenter as instructors and C. W. Cutler and F. J. Leviseur as clinical assistants. Thus was launched on its enviable career a great factor in the postgraduate instruction of dermatology in America.

George Henry Fox, the head of the new department, had already gained a high reputation in his specialty. He was at the head of his own service at the New York Skin and Cancer Hospital and was also

professor of dermatology at the College of Physicians and Surgeons. He had already published his celebrated "Photographic Atlas of Diseases of the Skin" and had been one of the principal founders of the American Dermatological Association in 1876. An anecdote which he related to me and which appears in his delightful "Reminiscences" [1] refers to the New York Post-Graduate Medical School and Hospital and belongs in this relation.

> On Thanksgiving Day a "spread" was prepared for the students. Around the large lecture room were two rows of arm chairs and in the center a table was laden with turkey, sandwiches, etc. Doctor Roosa urged a number of the faculty to be present on this occasion and act as a reception committee. I was on hand promptly and while my inclination was to talk with Rice, Sturgis, and others, I felt it my duty to try and be as agreeable as possible to some of the students who were strangers to me. Seeing a vacant chair in the circle I took it and began a conversation with the doctor at my left. He proved to be from Montana and entertained me with an interesting account of the mining industries there and of his wife and children. Then it occurred to me that the doctor at my right who was silently stowing away a plate full of salad might perhaps feel slighted if I did not pay him a little attention. So I turned and inquired as pleasantly as possible "Are you from the West?" Swallowing a spoonful of salad he slowly and scornfully said, "No, I am the Second Assistant in the Orthopedic Department." Great Heavens, what should I do to repair such a humiliating blunder. But before I could frame the proper apology he turned to me and to my great surprise asked "Where are you from?" As Vice-President of the institution I was paralyzed for the moment, but quickly realized that my friend had evidently studied at some other college than the "P and S." and not being interested in dermatology we were both in the same boat, neither one of us having ever seen or heard of the other.

Dr. Fox died on May 3, 1937, in his ninety-first year, and in his long span of life he had received a host of dermatologic honors. Besides his great friendliness, sociability and joviality, he had another but much rarer attribute, namely, modesty. On the many occasions that we were together I have never heard him speak of his own honors, but he was always ready to speak of those around him who had attained a high degree of proficiency in the specialty he had so greatly loved. Another of Fox's most lovable traits was the extraordinary friendship and interest which he manifested for the young tyros of his specialty. His willingness to help them in every way possible was expressed without the slightest trace of condescension. As Pusey rightly stated, "He was perhaps the friend of more American dermatologists than any other one of his generation." After Dr. Fox had spent some years as professor and vice president at the New York Post-Graduate Medical School and Hospital a serious disagreement arose as to the management of its affairs, and Dr. Fox resigned.

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1. Fox, G. H.: Reminiscences, New York, Medical Life Press, 1926.

He was succeeded by Dr. Robert W. Taylor, one of the organizers of both the New York Dermatological Society and the American Dermatological Association. Known to his intimates as "Bob" Taylor, he was a man of forceful opinions and a born fighter. He was such an avid reader of current literature that he could not only quote authors but give their opinions verbatim. He had a remarkable memory and could frequently relate years later clinical histories of patients, even recalling their names. In discussions he was fond of high-sounding names and particularly liked the word "epiphenomenon." Because of his extraordinary memory and complete knowledge of the current literature, he must have made a splendid teacher.

Dr. George T. Elliot was next in line as head of the department. He deserved the honor, as he had served as an assistant from the inception of the service under Professor Sturgis. He later became professor of dermatology and syphilology at Cornell University and from 1882 to 1901 was Dr. L. Duncan Bulkley's chief of clinic at the New York Skin and Cancer Hospital. Dr. Charles W. Allen (1854 to 1906) also served as professor of dermatology. He devoted much attention to roentgenotherapy and phototherapy and paved much of the way for others in those respective fields. He was jovial and had an overflowing good humor. He died prematurely at Gibralter while on his way home from the Fifth International Dermatological Congress at Lisbon, to which he was a delegate from the American Dermatological Association.

Dr. Sigmund Pollitzer (1859 to 1937) served the school as professor of its department of dermatology from 1895 to 1915. He was an outstanding figure in the dermatologic world. Pollitzer was graduated from the college of Physicians and Surgeons of Columbia University in 1884. After graduation he left for Europe and did research work in physiology in Heidelberg, Germany, and bacteriology in Fresenius' laboratory in Weisbaden, Germany; later he took up special work in Virchow's laboratory and at this time did much original work in physiologic chemistry. It was not until 1889 that he entered on his life's work, first at Unna's clinic and then as an assistant to Sir Malcolm Morris, where for a time he edited the *British Journal of Dermatology* under Morris' direction. From London he went to Paris, and there began a life-long friendship with Darier, whose textbook he translated into English in 1920. Pollitzer made approximately seventy-one contributions to dermatologic literature. Among the best remembered are his monographs on acanthosis nigricans, xanthoma of the eyelid, hydradenitis suppurativa, parakeratosis variegata, arsphenamine for the treatment of syphilis and serum therapy and serum diagnosis in syphilis. Pollitzer was an expert histopathologist. He was a strict parliamentarian and was especially critical of long-winded discussions lacking concrete facts. In such instances he could in a few words of polished

English and in well chosen scientific terms completely smother the unhappy speaker with unassailable facts, from which there was nothing else to do than to retire in confusion. Pollitzer in acting thus did much good service, for he deflated the ego of the usual group of know-it-alls who frequent every dermatologic meeting. In his home and with his friends he exuded kindness, generosity and simplicity. Despite his honors and his high ability, he was always the earnest student. Pollitzer belongs to that small group of physicians who have placed dermatology on a sound, dignified and scientific basis. I have always considered the friendship Pollitzer evinced for me one of the great satisfactions of my life. He is sadly missed at the meetings of the Section of Dermatology and Syphilology of the New York Academy of Medicine, to which organization he was devotion itself.

Dr. A. Schuyler Clark (1874 to 1929) was for nine years a professor in the department of dermatology at the school. He and Dr. Henry H. Whitehouse (1864 to 1938), who served as professor and executive officer of the department from 1914 to 1925, furnish additional evidence of the cordial relations existing between the New York Post-Graduate Medical School and Hospital and the New York Skin and Cancer Hospital, as both men were active in Dr. Bulkley's service at the latter institution. Dr. Whitehouse succeeded Dr. George Henry Fox at the New York Skin and Cancer Hospital as head of one of the clinics there. He served for thirty-eight consecutive years at that hospital and eleven years at the New York Post-Graduate Medical School and Hospital. In addition, he was elected president of the medical board of the New York Skin and Cancer Hospital in 1928 and served for seven years. Whitehouse greatly enjoyed teaching, and his lectures were carefully prepared and lucidly presented to the matriculates, who always listened to them attentively. He was a fine clinician and skilled in therapy, a fact easily appreciated in consideration of the thirty-eight years spent in the largest dermatologic clinic in America under the tutelage of physicians like L. Duncan Bulkley, George Henry Fox and George T. Elliot. Whitehouse's personality was delightful. At the dinner table, in debate, while teaching and in conversation, whether dermatologic or lay, he was always refreshing and affable. He was a staunch friend, and if he did dislike any one it was for a logical reason and he did not hesitate to give vent to that reason to the man himself. At the time of his death he was the senior member of the New York Dermatological Society, which he had served as president for three different terms. He is greatly missed by those who were his intimates.

The year 1928 marked a new era for the department of dermatology and syphilology at the New York Post-Graduate Medical School and Hospital. When Whitehouse resigned in 1925, A. Schuyler Clark became the head of the service and remained in that institution until

1928. In the meantime, Dr. John A. Fordyce died on June 4, 1925, and George M. MacKee, who had been his chief of clinic at New York University and had followed him as chief of clinic at the College of Physicians and Surgeons, had built up a splendid dermatologic organization at the Vanderbilt Clinic, more than doubling the attendance of patients at the clinic, thereby giving it a world-wide reputation. Every one expected that MacKee would succeed Fordyce as professor of dermatology and syphilology at the College of Physicians and Surgeons, as he had built up a clinic second to none in the United States, had himself done an enormous amount of original work and occupied an enviable position in the dermatologic world, but politics ordered otherwise, and he did not receive the appointment. He and his staff stuck to the service until well beyond the appointment of Fordyce's successor, whereupon he and most of his staff resigned from the Vanderbilt Clinic. Dr. A. Schuyler Clark resigned his post at the New York Post-Graduate Medical School and Hospital, and MacKee and his original Vanderbilt Clinic staff took it over. The change took place in 1928. In their first year eighteen postgraduate students matriculated. MacKee, a born organizer, soon had the clinic running at top efficiency, and the increase in the reputation of the department caused a great increase in matriculates. At the time of the affiliation with the New York Skin and Cancer Hospital in 1934, MacKee was the logical choice as director of the combined institutions. The entire main building of the Stuyvesant Square Hospital was renovated and altered in order to create a complete self-contained dermatologic unit. The building consists of four stories and a basement. In the basement the roentgenotherapy, phototherapy, physical therapy and photographic departments are located. On the first floor are the offices, the reception rooms for patients, the files and the department of syphilology. The second floor is devoted to new patients, a large air-conditioned lecture hall, with ample dressing rooms, and the office of the chief of clinic. The third floor houses the old patients, dressing rooms and the department of allergy. On the fourth floor are the surgical department, the department of mycology and the histologic laboratory. It will therefore be seen that the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital is a complete unit, in which all divergent branches of dermatology, investigative and otherwise, can be studied and cared for under a single roof. Dermatologic beds are taken care of in two wards of the hospital, which are exclusively for dermatologic use.

Thus the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital has entered on a phase which can but enhance the previous splendid record of dermatologic accomplishment made by the United States as a whole, but one must keep in mind that,

after all, these accomplishments would amount to little, were it not for the ground work done by pioneers of yesterday, who in turn received the flaming torch of dermatologic knowledge from Biett, Cazenave, Devergie and Bazin of France, Willan, Bateman, Wilson and Tilbury Fox of England, Unna of Germany and that immortal master, Ferdinand von Hebra of Vienna, and his associates Auspitz, Kaposi and Neumann. To them, after all, remains the glory of molding American dermatology, which today has grown to lusty manhood, stands on its own feet, and in teaching, research and clinical facilities is second to those of no country in the world.

THE VESICANT CHEMICAL WARFARE AGENTS

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In the World War there were introduced irritant chemical compounds which acted primarily by blistering the skin or mucous membranes. Although known to chemists since 1866, it was not until July 22, 1917 that the first compound, dichloroethylsulfide (mustard gas), was used on a large scale as a casualty-producing agent. Within three weeks after the introduction of this gas by the Germans, the British forces had 14,276 members injured, of whom 500 died.[1] In the American Expeditionary Forces in the World War there were 27,711 casualties from mustard gas, with only 599 deaths. Of this large number of casualties there were only 4 cases of loss of sight of both eyes.[2] Whether the blindness was due to mustard gas or to other gases in all of these 4 cases is not known. Although primarily sternutators, some of the other war gases, such as diphenylchloroarsine (Clark I), phenyldichloroarsine, ethyldichloroarsine (Dick), diphenylcyanoarsine (Clark II) and methyldichloroarsine (Methyldick), also blistered the skin. There is some controversy as to whether the efficient methyldichloroarsine was used actually in warfare toward the end of the war.[3]

At the Ninth International Congress of Military Medicine and Pharmacy, in Bucharest, Rumania, in June 1937, it was claimed, "It is likely that in future war the use of gas will be made on a larger scale."[4] Flury[5] has stated that the subject of the chemical warfare agents "will present to the dermatologist a good many unsolved questions and will stimulate him to concern himself more with this field."

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1. Prentiss, A. M.: Chemicals in War, New York, McGraw-Hill Book Company, Inc., 1937.

2. Gilchrist, H. L.: A Comparative Study of World War Causalties from Gas and Other Weapons, Washington, D. C., Government Printing Office, 1928.

3. Sartori, M.: The War Gases, New York, D. Van Nostrand Company, Inc., 1939.

4. Bainbridge, C. W. S.: Report on Ninth International Congress of Military Medicine and Pharmacy, Mil. Surgeon **82**:225 (March) 1938.

5. Flury, F.: Dermatologische Probleme im Luftschutz, Med. Klin. **30**:13 (Jan. 5) 1934.

CLASSIFICATION

There are many vesicant agents, but because of the military tactical requirements and the limitations of manufacturing and of transportation facilities, there are at present relatively few that meet all these requirements. From a physiologic aspect these vesicant gases may be classified briefly as causing (1) primarily local tissue irritation (the sulfur compounds) and (2) combined local irritation and systemic intoxication (the arsine compounds).

Dichloroethylsulfide is known as mustard gas to the Americans and English, as yperite to the French and as *"Senfgas,"* mustard gas or *Lost* to the Germans. *Lost* is derived from the first two letters of the names of the German investigators of this gas (Lommel and Steinkopf). Mustard gas and lewisite (chlorovinyldichloroarsine) are known to the Germans also as *Gelbkreuzegruppe,* because of the manner of marking the shells containing these gases. On the basis of the rapidity of production of bullae, the severity of the local reaction and the time required to heal the local lesions, Prentiss [1] has classified the gases in descending order:

(1) mustard gas
(2) lewisite
(3) phenyldichloroarsine
(4) methyldichloroarsine
(5) ethyldichloroarsine
(6) phenyldibromoarsine
(7) dibromethylsulfide

Unlike those war gases which cause primarily severe damage to the lung, such as phosgene (carbonyl chloride) and trichlormethylchloroformate (Perstoff), most of the vesicant agents have the important physical characteristic of persistence, i. e., the chemicals remain in the place where they are discharged for some time. For instance, mustard gas, because of its low volatility, can remain in the summer for five to ten days in the open and from two to three weeks in the woods; in the winter the gas can remain for several weeks both in the open and in the woods. Mustard gas, when pure, freezes at 14 C. (57 F.). Because of this fact the presence of the mustard gas may not be detected in cold weather. In addition to temperature, other elements of weather, such as wind, clouds and air pressure, have some influence on the concentration of mustard gas vapor. Mustard gas will penetrate paint, woodwork, porous materials, shellac, paper, wax, leather and ordinary clothing. Oilskin clothing and synthetic rubber materials are penetrated slowly. Metals, glass, glazed earthenware and cellulose coverings are

resistant to the gas. The presence of mustard gas on a person or object is spoken of as "contamination." The persistence of dibromethylsulfide on the ground is said to be greater than mustard gas only in dry weather. No definite data are available on the persistence of diiodethylsulfide.

Physical Properties of the Vesicant Gases

Agent	Physical State	Odor	Volatility at 20 C. (68 F.)	Solubility	
				Water	Other Solvents
Mustard gas	Oily liquid; brownish, colorless when pure	Garlic or horseradish	0.625 mg. per liter	0.047 Gm. per liter 0.069 Gm. per liter (25 C.)	Very soluble in various hydrocarbons and organic solvents (kerosene, gasoline, absolute alcohol, carbon tetrachloride, chloropicrin, petrolatum and paraffin wax)
Dibromethylsulfide	White crystals, melting point 310-340 C.	?	400 mg. per liter	Insoluble	Soluble in alcohol, ether and benzene
Diiodethylsulfide	Bright yellow prisms, melting point 62-68 C.	?	?	?	?
Lewisite	Colorless liquid	Geranium	2,300 mg. per liter	0.50 Gm. per liter	Readily soluble in benzene, absolute alcohol, olive oil and kerosene
Ethyldichloroarsine	Liquid; colorless first, then slightly yellow	Fruity	20,000 mg. per liter	1.00 Gm. per liter	Readily soluble in alcohol, ether, benzene and acetone
Methyldichloroarsine	Colorless liquid	?	74,440 mg. per liter	1.00 Gm. per liter	Soluble in ordinary organic solvents
Phenyldichloroarsine	Liquid; colorless when pure, then yellow	?	404 mg. per liter	Insoluble	Soluble in ordinary organic solvents
Diphenylchloroarsine	Dark brown liquid	Shoe polish	0.69 mg. per liter	2.0 Gm. per liter	Readily soluble in carbon tetrachloride, phosgene, chloropicrin and phenyldichloroarsine. 20 Gm. per 100 cc. absolute alcohol [3]; 50 Gm. per 100 cc. kerosene; 100 Gm. per 100 cc. benzene; 14 Gm. per 100 cc. olive oil
Diphenylbromarsine	White crystals	Similar to diphenylchloroarsine			
Diphenylcyanarsine	Colorless prisms	Mixed garlic and bitter almonds	0.0002 mg. per liter	Sparingly	Readily soluble in alcohol, benzene, chloroform and ether
Diphenylaminechloroarsine	Green or brownish solid	Practically odorless	0.02 mg. per liter	Practically insoluble	Sparingly soluble in organic solvents

Lewisite as such is much less persistent than mustard gas; it lasts in the summer only twenty-four hours in the open and one week in the woods. The persistence of the other chlorvinyl arsines has not been reported. The aromatic arsines are nonpersistent, the significant concentrations lasting several minutes to several hours.

Hydrolysis is important from both a military and a medical standpoint, for hydrolysis may render the agent, after a period, either harmless or still dangerous. The latter result is produced by a hydrolysis product

being of itself toxic. Mustard gas in contact with water is sparingly soluble. It hydrolyzes at a rate depending on the temperature and the rate of stirring. The hydrolysis products are hydrochloric acid and thiodiglycol. In contrast to mustard gas, lewisite is rapidly decomposed in contact with water even at ordinary temperature, with the formation of hydrochloric acid and an oxide of lewisite, which itself is nonvolatile and vesicant. Dibromethylsulfide is more rapidly decomposed by water than dichloroethylsulfide. The hydrolytic activity of diiodethylsulfide is not reported at present. The aromatic arsines hydrolize easily, producing nonvesicant but nauseating arsenic trioxide compounds.

To be able to recognize these vesicants and to understand their action and the therapy of the lesions produced, it is necessary to know more of the various physical properties of the gases. As a rule, whenever mustard gas is in sufficient concentration to be recognized by its characteristic odor casualties may be caused by exposure over prolonged periods.

CLINICAL SYMPTOMS

The clinical picture of the conditions caused by this vesicant group as a whole may be divided into the following stages: (1) the latent period, (2) the period of acute reactions and (3) the period of subacute and chronic reactions.

The duration and intensity of the reactions vary according to the character and concentration of the chemical agent used, the sensitivity of the patient and, for the skin, the area or areas of skin involved. Actual war experience has given the picture of the lesions caused by mustard gas and some of the aromatic arsines; the lesions produced by the aliphatic arsines and other compounds have been studied chiefly through various experimental procedures. Apparently no new types of vesicants were used in the Italo-Ethiopian War.

In regard to the clinical course of the mustard gas burn, the latent period is an important phase, because it is only in this stage that the treatment may prevent or reduce appreciably in severity any subsequent lesions. The latent period varies for mustard gas from about two to six hours. Generally, the longer the latent period the less severe will be the subsequent reaction. During this phase the mustard vapor or liquid remains on the cutaneous surface approximately three minutes, depending on the amount. Then it is slowly absorbed (through great solubility in cutaneous lipids ?). The deep penetration into the skin is said to occur through the follicles and the sebaceous glands. Absorption is more rapid and more intense if the cutaneous surface is covered and if the skin itself is warm and moist. The end of the latent period is marked by burning and itching.

Erythema is the first sign of the period of reaction. It occurs especially in the axillary and crural areas and on the scrotum, neck, elbows and eyelids and may be faint or intense. Erythema may be the only reaction and may subside entirely in twenty-four hours.[6] Nikolsky's sign may be obtained at times over the erythematous areas. However, the more common course is for vesicles and bullae to develop gradually after eight to twelve hours. The height of the bullous reaction is two and a half to three days. Secondary infection is not uncommon. The fluid from the bulla does not of itself produce fresh vesicles. In lesions caused by the drops or splashes of the liquid chemical and not by the vapor, the vesicles are arranged in a characteristic peripheral fashion about a central area of induration. Around the vesicles may be found an irregular zone of whitish discoloration (*der anämische Bezirk*).[7]

The raw, oozing surfaces heal slowly. The scar is usually smooth. Contractures may occur in scarring over joint surfaces. Various forms of pyoderma are not uncommon during the subacute and chronic phases. Even with the extensive cutaneous lesions caused by mustard gas itself there are usually no systemic reactions save vague malaise, anorexia, low grade fever and a decreased amount of hemoglobin in the blood. Of course, in this subacute and chronic phase secondary infection of the cutaneous lesions themselves may occur and produce the usual symptoms and signs of sepsis. In the postmortem study of victims of uncomplicated mustard gas poisoning, essentially nonspecific toxic changes have been found in the viscera.

Interesting also to dermatologists is the fact that widespread brownish pigmentation may occur, following even mild erythema, and may last for weeks. It is reported that the brownish pigmentation may arise also without preceding erythema, and occasionally this form of discoloration may be distributed over the body in large irregular blotches.[7] Severe pruritus may be present for some time after all lesions have healed. Under certain rare circumstances mustard gas may produce such a deep burn of the skin that no bulla is formed. The ulceration so resulting may require months to heal. Although it is frequently not possible to classify them, Muntsch [7] stated that there are four general types of cutaneous reactions: (1) simple erythematous; (2) pigmented and exfoliative; (3) eczematous, and (4) edematous, bullous, ulcerative and necrotizing.

Microscopically, the earliest changes in the epidermis are distortion and shrinkage, and in the cutis, dilatation of the vessels, with some perivascular infiltrate and edema of the pars papillaris. From the histologic study of cutaneous lesions one-half hour after the application of

6. An Atlas of Gas Poisoning, London, His Majesty's Stationery Office, 1938.

7. Muntsch, O.: Leitfaden der Pathologie und Therapie der Kampfstofferkrankungen, Leipzig, Georg Thieme, 1939.

mustard gas, Warthin and Weller [8] stated, "in the neighborhood of the hair follicles the corium is affected more deeply than elsewhere, showing a distinct penetration through the hair follicles." Following these changes spongiosis develops. Definite intraepidermal vesicles may be seen in two hours. The inflammatory infiltrate in the cutis increases, and many eosinophils [7] are found. The necrotic changes in the epidermis continue, and soon extensive crusting is produced. There may be considerable hemorrhage in deeper tissues, but vessel thromboses are not great and occur chiefly at the edge of the ulceration of the skin. In the healed area the pigmentation is found to be chiefly chromatophore. In a necrotic cutaneous lesion from a patient who died of mustard gas burns Warthin and Weller [9] noted sebaceous gland necrosis, with islands of regenerating squamous epithelium marking the site of these glands. The other significant feature of a picture of essentially severe and deep destruction of skin with attempts at regeneration was a sparse inflammatory infiltrate save where secondary infection was present. Rehbein [10] has commented on the histologic similarity of the bullae caused by mustard gas and those of pemphigus. From a study of animal experimentation Dörffel and Pöpping [11] were impressed with the close histologic association of mustard gas dermatitis and acute roentgen dermatitis. They found no similarity of mustard gas dermatitis to severe acid burns of the skin. They mentioned, in addition, dyskeratotic changes in the healing phase. Such changes have not been described for the human skin. There have been no reports of a tendency toward malignancy in mustard gas lesions. Moreover, Visser and Seldam [12] succeeded in inhibiting malignant growth from tar in mice by adding 0.5 per cent mustard gas to the tar. The anticarcinogenic activity of mustard gas had been noted also by Berenblum and Wormall [13] and by Jány and Sellei.[14] It is interesting also that mustard gas solutions injected subcutaneously, intramuscularly and intraperitoneally cause locally only intense edema and no necrosis. The reason for the absence of local

8. Warthin, A. S., and Weller, C. V.: The Pathology of the Skin Lesions Produced by Mustard Gas (Dichlorethylsulphide), J. Lab. & Clin. Med. **3**:447 (May) 1918.

9. Warthin, A. S., and Weller, C. V.: The General Pathology of Mustard Gas (Dichlorethylsulphide) Poisoning, J. Lab. & Clin. Med. **4**:265 (Jan.) 1919.

10. Rehbein, cited by Muntsch.[7]

11. Dörffel, J., and Pöpping: Tierexperimentelle Untersuchungen über die Veränderungen der Haut nach Aetzung mit Dichloriäthylsulfid (Gelbkreuz) und Mineralsäuren, Virchows Arch. f. path. Anat. **295**:1, 1935.

12. Visser, J., and Seldam, R. E. J., cited by Schwartz and Tulipan.[33]

13. Berenblum, I., and Wormall, A.: The Immunological Properties of Proteins Treated with BB′ Dichlorodiethylsulphide (Mustard Gas) and BB′ Dichlorodiethylsulphone, Biochem. J. **33**:75 (Jan.) 1939.

14. Jány and Sellei, cited by Berenblum and Wormall.[13]

necrosis is thought to be rapid local absorption of the irritant, unlike the slow absorption which occurs in the skin.[15]

Since mustard gas is universally irritant, lesions of any unprotected surface may occur. The commonest of these is in the eye, where the conjunctivitis varies from simple acute to chronic proliferative. There is described a xanthoma-like pigmentation which develops near the outer or inner sclerocorneal junction or over the corneal limbus.[16] There may be severe body burns without eye burns if the eyes have been protected by a good gas mask. Ulceration of the lips, tongue and pharynx may occur also. Small burns in the mouth and on the tongue resemble aphthous ulcers. Laryngitis with long-continued hoarseness may result also. If a sufficient concentration is inspired, an ulcerative tracheobronchitis with secondary severe bronchopneumonia may occur. It is bronchopneumonia which is chiefly responsible for the deaths from mustard gas.

The effects of lewisite differ essentially from those of mustard gas in that the latent period is much shorter (fifteen to thirty minutes); there may be associated sneezing and nasal irritation; the bullae increase in size more rapidly; the contents of the bullae are clearer, and secondary infection of the bullae is much less frequent. In addition, because of the arsenic content, varying degrees of arsenical poisoning are produced by the cutaneous lesions caused by lewisite. Vedder[17] claimed that a man of average weight would die if 1.4 cc. of lewisite were splashed on his skin and he received no treatment. The pigmentation following lewisite lesions is believed by some to be more intense than that following mustard gas lesions.[18] On the other hand, Héderer and Istin[19] stated that in the absence of secondary infection, the lewisite lesion may heal with little or no pigmentation. Other arsenical warfare agents also act more quickly than mustard gas. The differences between the various arsenicals are essentially quantitative. Ethyldichloroarsine produces paronychia more commonly than the other agents.

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15. Smith, H. W.; Clowes, G. H. A., and Marshall, E. K., Jr.: On Dichlorethylsulfide (Mustard Gas): IV. The Mechanism of Absorption by the Skin, J. Pharmacol. & Exper. Therap. **13**:1 (April) 1919.

16. Warthin, A. S.; Weller, C. V., and Herrmann, G. R.: The Ocular Lesions Produced by Dichlorethylsulphide (Mustard Gas), J. Lab. & Clin. Med. **4**:785 (Oct.) 1918.

17. Vedder, E. B.: The Medical Aspects of Chemical Warfare, Baltimore, Williams & Wilkins Company, 1925.

18. Hanzlik, P. J., and Tarr, J.: The Comparative Skin Irritant Properties of Dichlorethylsulphide ("Mustard Gas") and Other Agents, J. Pharmacol. & Exper. Therap. **14**:221 (Nov.) 1919.

19. Héderer, C., and Istin, M.: L'arm chimique et ses blessures, Paris, J. B. Baillière et fils, 1935.

MECHANISM OF THE ACTION OF VESICANTS

The actual mechanism of how these vesicants react with the cells is still unknown. There are, of course, some theories. The oldest one is that of hydrolysis, namely, that the mustard gas is absorbed into the cell, where hydrolysis occurs, and there are formed thiodiglycol, which is inert, and hydrochloric acid, which destroys the cell. However, briefly, neither clinically nor histologically does the cutaneous lesion due to mustard gas resemble a burn due to strong acid. Another theory mentioned by Flury and Zernik [20] is that the intracellular destruction is brought about by oxidation and that other types of foreign body products are formed. They also suggested the possibility that mustard gas acts directly as a capillary toxin, producing dilatation and increased permeability. There is no definite proof for such wide generalizations. The relatively recent theory is that of Cashmore and McCombie,[21] which claims that the cutaneous lesions are produced by a combination of the mustard gas and the "amino acids present in the skin."

SENSITIVITY OF THE SKIN TO VESICANTS

Every one is agreed that persons vary in their sensitivity to the vesicants, especially to mustard gas. For experimental work either suitable dilutions of the liquid material or the vapor has been used. The liquid has been dropped on the skin by means of a graduated pipet or a fine glass rod. Vapor exposures were made by means of the blower system (quantitative) of Hanzlik and Tarr [18] or simply by placing the cutaneous surface over the mouth of a test tube, which is kept at constant temperature and contains cotton plugs soaked with the material. This is similar to the method of Machle and Zwick [22] for testing the skin to gasoline vapors. The "Dunstprobe" method of Miescher [23] could be used for the study of the effect of mustard gas vapor on the skin. In general, the vapor tests have been preferred because the results are more uniform and milder. For the concentration of the solution for direct application to the skin, the titer varies usually from 1 : 10,000 to 1 : 100. With 0.01 per cent solution approximately 2 to 3 per cent of white men are found to be "hypersensitive" and 20 to 40 per cent "resistant." [24]

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20. Flury, F., and Zernik, F.: Schädliche Gase, Berlin, Julius Springer, 1931.

21. Cashmore and McCombie, cited by Berenblum and Wormall.[18]

22. Machle, W., and Zwick, K. G.: Gasoline Dermatitis, M. Bull. Univ. Cincinnati **7**:93 (Nov.) 1935.

23. Miescher, G.: Die Dunstprobe beim Ekzem, Schweiz. med. Wchnschr. **70**:93 (Feb. 3) 1940.

24. Marshall, E. K., Jr.; Lynch, V., and Smith, H. W.: On Dichlorethyl-Sulphide (Mustard Gas): II. Variations in Susceptibility of the Skin to Dichlorethylsulphide, J. Pharmacol. & Exper. Therap. **12**:291 (Dec.) 1918.

Expressed quantitatively by Sartori,[3] the average amount of mustard gas for the production of an erythema is 0.12 mg. per square centimeter of skin and for a vesicle, 0.5 mg. per square centimeter of skin. With 0.01 per cent solution 78 per cent of Negroes do not react. Ferri [25] found that sun-tanned skin was less sensitive than the untanned skin. Even with high dilution of mustard gas the conventional technic of patch test has not been used. As previously indicated, the cutaneous areas that are relatively thin skin, moist and subject to friction are more sensitive to mustard gas. Ferri [25] claims in addition that the skin is more sensitive in summer than in winter. It seems to us that the reason for the differences in intensity of the cutaneous reactions in various areas of the same person may be due to differences simply in the concentration of the mustard gas in those areas. Evaporation of the mustard gas from the cutaneous surface may be prevented by clothing or by the proximity of adjacent cutaneous surfaces and moisture. Repeated exposures to even minute quantities of mustard gas cause a gradually increasing sensitivity to mustard gas; this hypersensitivity may last for some years. This suggests certainly that mustard gas is a strong eczematogenous agent. Among the animals, the guinea pig, dog and rabbit react within the same ranges as man. Data on the horse are conflicting. By means of precipitin and complement fixation tests in rabbits, Berenblum and Wormall [13] found that protein changes were produced by a reaction at room temperature between BB′ dichlorodiethylsulfide (mustard gas) and horse serum and between BB′ dichlorodiethylsulfone and horse serum. There were no serologic cross reactions between the sulfide-treated and the sulfone-treated proteins. These experiments are some proof for the amino acid theory of the action of mustard gas. The contents of the bulla due to mustard gas have not been used for passive transfer tests.

There has been considerable less work done with the arsines. There are no data available as yet concerning the arsenic sensitivity of the skin following burns with lewisite. With phenyldichloroarsine Sayers and Dudley [26] found that a 1 per cent solution (in heavy oil) caused a severe reaction on the skin of the majority of a relatively small group tested.

THERAPY

The diagnosis of mustard gas poisoning is made usually by the characteristic odor of the vesicant, brownish oily stains present on the clothing and the patient's history. At present there are no good specific

25. Ferri, G., cited by Schwartz and Tulipan.[33]

26. Sayers, R. R., and Dudley, H. C.: Toxicology of Phenyldichlorarsine, Pub. Health Rep. **53**:1292 (July 29) 1938.

chemical indicators which are simple to use. For effective therapy the diagnosis must be made as soon as possible.

From their persistence and penetrating power in clothing and leather, the vesicants deserve the title "chemical lepers." The gas mask will protect only the eyes and the respiratory tract. Therefore, the chances for cutaneous lesions are high. The physician caring for the patients is in great danger of being poisoned himself unless he is protected from vapors by a gas mask and from contaminated clothing and skin by special oilskin gloves and clothing. For military purposes clothing can be rendered resistant to mustard gas, but this cannot be used on a wide scale, especially in civilian life. The protective costumes at present are cumbersome and do not permit exertion for any long periods of time. The use of protective salves and pastes, such as chlorine mixtures, glycerol [27] and cellulose, have not been proved effective or practical. The therapeutic agents used chiefly for early treatment are the solvents mentioned in the tables or oxidizing materials. The oxidizing agents are various chlorine preparations, such as bleaching powder, chloramine-T, diluted solution of sodium hypochlorite and hydrogen peroxide and permanganate.[28] One great difficulty with all chlorine preparations is their more or less rapid loss of chlorine. If the patient can be seen before the cutaneous absorption occurs (three minutes), the skin must be washed with the solvents or, next best, with soap and water, and the washing rags must be discarded and decontaminated. The decontamination of cloth, including bandages (mixed vesicant and shell wounds), can be done by burning, boiling, mixing with solution of sodium hypochlorite, chlorination or exposure to freely circulating air for long periods (summer two to seven days; winter fourteen days). Instruments may be decontaminated by cleansing with methyl alcohol and then boiling.

The patient will be seen usually in the latent period. At this stage therapy should be instituted, since it may reduce the severity of the irritation. The clothing should be removed and the skin washed with the solvents or oxidizing agents, and if there has been no protection of the eyes they should be irrigated with 0.5 to 1 per cent chlorcosane solution of dichloramine-T, followed by boric acid; [16] if the chlorine solutions are not available, a mild alkaline salve may be used. The mouth should be rinsed and the throat gargled with warm sodium

27. Klarenbeek, A.: Protection of the Skin Against Mustard Gas by Means of Cellulose Preparations, Nederl. tijdschr. v. geneesk. **81**:5905 (Dec. 11) 1937; abstracted, J. A. M. A. **110**:618 (Feb. 9) 1938.

28. Hillman, C. C.: Care of Gas Casualties, Mil. Surgeon **70**:529 (June) 1932.

bicarbonate solutions. The patient must then be watched for twelve hours. The oxidizing agents used ordinarily are:

1. Bleaching powder paste, made with equal parts of water. Rinse from the skin to avoid irritation. So-called bleaching powder cream may also be used, 2 parts of bleaching powder to 1 of white petrolatum (of questionable value but recommended in several European countries). Bleaching powder still remains the chief therapeutic agent.
2. Chloramine-T, 1 to 2 per cent.
3. Diluted solution of sodium hypochlorite, 0.5 per cent (fresh). Watch the skin for irritation.
4. Hydrogen peroxide, 2 to 3 per cent.
5. Potassium permanganate, 1 : 1,000 to 1 : 10,000.

The value of ferric hydroxide pastes (freshly prepared) for use against the arsines is doubtful. The Germans believe them to be worthless. Sayers and Dudley,[26] however, have shown experimentally in a small group that this material does have some protective value against phenyldichloroarsine. Their mixture was made of equal parts of petrolatum and freshly precipitated ferric hydroxide. Vedder's[17] mixture was 6 parts of ferric hydrate to 1 of pure glycerin; he claimed that it was permanent if kept in air-tight containers.

Even when the actual erythema has occurred, treatment should be continued. When the bullae appear, they should be débrided, since those caused by mustard gas are especially prone to infection. From the experience of the Dutch Ambulance Service[29] in the Italo-Ethiopian War it seemed that tannic acid (3 to 5 per cent) did work in the bullous stage. Although it has not been used, it appears as if the compound solution of tannic acid[30] would be more practical and, of course, more stable. Silver nitrate (10 per cent) could be used after the application

29. Belmonte, A. C., and Winkel, C. W. F.: With the Ambulance of the Netherlands Red Cross in Ethiopia, Nederl. tijdschr. v. geneesk. **80**:3289 (July 11) 1936; abstracted, Schweiz. med. Wchnschr. **48**:1216 (Nov. 28) 1936.

30. Fantus, B., and Dyniewicz, H. A.: Compound Solution of Tannic Acid, J. A. M. A. **109**:200 (July 17) 1937.

Potassium chloride	0.42 Gm.
Calcium chloride	0.80 Gm.
Salicylic acid	1.00 Gm.
Sodium chloride	10.50 Gm.
Tannic acid	100.00 Gm.
Distilled water, to make	1,000.00 cc.

Mix and permit to stand with occasional agitation until dissolved and filter, if required to dispense a clear solution.

of tannic acid to promote more rapid crusting. For the treatment of the ulcers and necrotic areas in the latter phases of these chemical burns, the ordinary remedies may be used. Here, too, diluted solution of sodium hypochlorite may be good, especially for the necrotic tissue; the uninvolved skin should be protected with petrolatum gauze.

Unlike extensive burns of the skin, the patients with vesicant gas burns do not show anhydremia or significant changes in the blood chloride content. Therefore, only with conditions such as secondary sepsis and bronchopneumonia should the general remedies be given. For lesions due to the arsines, adequate fluid intake and intravenous administration of sodium thiosulfate (?) and dextrose may be given to prevent arsenical intoxication. Because of the relatively long and painful convalescence these patients are discouraged and depressed, and measures should be taken to keep up their morale.

When the case is complicated by fractures or gunshot wounds, the surgeon and his assistants must protect themselves from poisoning through contact or inspiring contaminated air. Decontamination of the wounds and extensive débridements are advised.

RESIDUA OF THE VESICANTS

As has been mentioned before, with the large number of casualties and relatively small percentage of fatalities, there is likewise a small percentage of residua. Since mustard gas has been used the most extensively in warfare, the following conclusions refer to it. Follow-up studies have been done in this country by Gilchrist and Matz.[31] The deep cutaneous burns heal with scars which in flexural areas may give rise to contractures. Some patients, percentage unknown, have had sensitive scars for a time. Occasionally, the pyoderma associated with the latter stages may persist for some months in the form of a stubborn furunculosis. With the same time relations, an eczematous condition may develop in some cases, while in others actual chronic dermatitis results from the vesicant. It is not known whether a polyvalent sensitivity develops also.

The small number of cases of blindness caused by mustard gas has been mentioned before. This is relatively much less than the blindness caused by other warfare missiles. Various other chronic deformities of the eyes may result. Chronic bronchitis and its concomitants may follow pulmonary irritation. Actually the incidence of this condition is much less than compensation figures indicate. Pulmonary tuberculosis does not follow, causally, any war gas poisoning. Although

31. Gilchrist, H. L., and Matz, P. B.: The Residual Effects of Warfare Gases: I. Chlorins; II. Mustard, United States War Department, Chemical Warfare Service, 1933.

theoretically gastroenteric ulcers and scarring may follow the ingestion of mustard gas, clinically, at least, such complications are not important. All in all, the "relative humanity" of this form of warfare is easily seen.

INDUSTRIAL HAZARDS IN THE MANUFACTURE OF GASES

Since these compounds are so dangerous, their manufacture is likewise dangerous to the worker. Cole, Driver, Bowen and Cooper [32] have recently described a study of 24 workers with cutaneous irritations from the arsines, especially diphenylchloroarsine, and from mustard gas. Idiosyncrasy was obvious even in the small series. Moreover, in 1 chemist urticaria developed from various arsines. The authors have emphasized the fact that cleanliness of the plant and training of the workers will do much to avoid cutaneous reactions. Workers must be trained not only in prevention of all forms of reaction but also in securing early therapy. Not only may there be cutaneous reactions from the war gases, but also contact dermatitis from the chemicals used in the manufacture of these gases.[33] Since these war gases are strong poisons, they will be used more and more in civil life for insecticides and the like. Sayers and Dudley [26] have mentioned the use of phenyldichloroarsine in oil as a wood preservative. This nonmilitary use of the chemical warfare agents will also give rise to cutaneous irritations which the dermatologist must recognize and prevent.

OTHER PROBLEMS

This review lists only some of the more important phases of the modern study of these vesicants. There has been no description of the lesions in horses and the difficulty of prophylaxis and therapy with these animals. Mustard gas casualties on shipboard present many additional problems.[34] The subject of mixed traumatic and vesicant wounds was mentioned only briefly; yet toward the end of the last war it was the custom to mix chemicals in many different types of artillery shells. Operating rooms in which patients with wounds due to mustard gas are treated must have special arrangements to protect both personnel and patients. Some of the chemicals used as "tear gases" may also produce vesicles. These chemicals are bromobenzylcyanide, acrolein, chloroacetophenone and phenylcarbylamine chloride.

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32. Cole, H. N.; Driver, J. R.; Bowen, S. S., and Cooper, G.: War Gases and Industrial Hazards in Their Manufacture, Arch. Dermat. & Syph. **39**:45 (Jan.) 1939.

33. Schwartz, L., and Tulipan, L.: A Text Book of Occupational Diseases of the Skin, Philadelphia, Lea & Febiger, 1939.

34. Anti-Gas Precautions for Merchant Shipping, Air Raid Precautions, Handbook no. 7, London, His Majesty's Stationery Office, 1936.

This paper does not include a review of cutaneous lesions from other war materials, such as the deep burns from incendiary bombs (made of iron and aluminum or of magnesium) and from phosphorus, which is used to produce smoke screens.

THE FUTURE OF THE VESICANTS

Vesicants as warfare agents will be discarded only when more efficient agents are produced. Mustard gas and lewisite are the most effective materials of today. In 1919 Hanzlik and Tarr [18] reported a study of some 70 vesicant agents which might be used in chemical warfare. At that time mustard gas had the greatest efficiency as a cutaneous irritant. Over twenty years later it still retains that leadership, followed closely by lewisite and the other arsines. No descriptions of new and essentially different compounds have been published recently, but progressive chemical research may soon produce others. The physician is at a disadvantage at present since, because of ignorance of the exact mechanism of reaction, he is forced to use inadequate symptomatic therapy. However, he must keep abreast of such research, since knowledge in advance will do much to dispel unnecessary fear and panic about these materials and will prevent casualties.

CONCLUSIONS

Dermatologists should concern themselves with the problem of vesicant chemical warfare agents, for there is much to arouse their interest in this field. The basic mechanisms involved, the factor of cutaneous hypersensitivities and systemic poisoning from the cutaneous lesions of the arsine group are but a few of the more important questions for the dermatologist. It is because of the various unknown elements about these agents that today there is no adequate defense against the action of the vesicants.

UNUSUAL SEROLOGIC REACTIONS DURING PREGNANCY

REPORT OF A CASE

LOUIS G. JEKEL, M.D.
PHOENIX, ARIZ.

The following case report is offered without comment.

Mrs. M. W., white, aged 37, presented herself to Dr. P. T. Brown for antepartum care on July 12, 1938. She had previously been pregnant five times and had given birth at term to 5 normal, healthy children. Her routine obstetric examination indicated that she was normal and healthy. The routine Wassermann and Kahn tests, however, gave positive results. The tests were repeated with the same results in the same laboratory and in a second laboratory. The patient was

Summary of Serologic Reactions of Patient During Pregnancy

Laboratory Number	Date	Results of Serologic Tests			
		Wassermann	Kahn	Kline	Eagle
1	7/12/38	+++	++	....	....
1	7/21/38	+++	++	....	....
2	7/19/38	Positive	Positive	....	....
3	9/ 3/38	Negative	Negative	....	....
3	9/ 9/38	Negative	Negative	....	....
3	9/15/38	+	++	....	....
4	9/20/38	++	+	++	....
5	9/20/38	Anticomplementary	Negative	....	Negative
5	10/ 3/38	Positive	Negative	....	Negative
6	9/24/38	Specimen contaminated and unfit			

then sent to me for blood tests in a third laboratory and for examination and advice. I found no evidence of syphilis. The fact is notable that her mother, father, brother, sister and husband were all known to have negative Wassermann reactions. Her personal history and physical examination offered no hint of syphilis. Those conditions that are said to produce biologically false positive serologic reactions for syphilis were not present. The Wassermann and Kahn tests in the third laboratory gave negative results. Blood samples were sent to three nationally known laboratories. A complete summary of the various tests is given in the table.

The patient was advised to submit to a short course of antisyphilitic treatment. This she refused to do. On Feb. 23, 1939 she was delivered of a 7½ pound (3,402 Gm.) girl. The baby showed no abnormalities and has progressed normally since birth. The results of Kahn and Wassermann tests on March 9 were reported "doubtful" for the mother and negative for the father and baby.

From the Section on Dermatology, Lois Grunow Memorial Clinic.

Clinical Notes

PURPURA DUE TO INJECTION OF ESTROGENIC SUBSTANCE

EARL L. LOFTIS, M.D., DALLAS, TEXAS

After a fairly thorough search of the literature I failed to find a report of a reaction to estrogenic substance similar to that of a patient I have under observation. Therefore, I believe her case will be of interest.

REPORT OF A CASE

Mrs. I. N., aged 44, consulted me three years ago for treatment of eczema limited to the forehead and purpura limited chiefly to the thighs. The latter lesions were bluish purple and varied in size from that of a dime to that of a 25 cent piece. The eruption had been present several days, and some of the lesions were fading and new ones were appearing. Close questioning revealed a history of weekly injections of an estrogenic substance. The dermatitis of the forehead proved to be of the contact type. The injections of estrogen were stopped for three weeks, and all the lesions disappeared except the faint outline of one of them. The injections were resumed and within twenty-four hours numerous lesions again appeared on the thighs. One of the lesions was fixed, fading slowly and leaving a permanent faint trace. Bleeding of the gums always accompanied the attacks. Repeated tests were made at intervals, with different doses of the estrogenic substance and with different vehicles. The result was always the same. Aqueous and oily solutions caused the same reaction, proving that the vehicle was not responsible for the eruption. Physical examination and laboratory tests, including complete studies of the blood, made when the eruption was present and also between attacks, have given negative results except for a basal metabolic rate of —16 per cent.

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CHEILITIS AND DERMATITIS FROM RESORCINOL AND A DERIVATIVE

H. J. TEMPLETON, M.D., OAKLAND, CALIF.

In 1932 I reported,[1] along with Lunsford, a series of cases of cheilitis and stomatitis from a toothpaste containing hexylresorcinol. Since then I have observed additional cases in which this condition was caused by the same toothpaste or by a mouth wash containing the drug. There have also been reports in the literature of dermatitis from resorcinol used in hair tonics and in rectal suppositories. I recently saw a patient who is sensitive both to resorcinol, which she used in a hair tonic, and to its derivative hexylresorcinol, which she used in

1. Templeton, H. J., and Lunsford, C. J.: Cheilitis and Stomatitis from ST37 Toothpaste, Arch. Dermat. & Syph. **25**:439-443 (March) 1932.

lozenge form. This patient came to me complaining of dermatitis of the ears and also of cheilitis and stomatitis. Her history and a strongly positive result of a patch test indicated that the dermatitis of the ears was caused by a hair tonic I had given her which contained 5 per cent resorcinol in alcohol. The stomatitis was apparently caused by lozenges containing hexylresorcinol ("sucrets"), as evidenced by a strongly positive reaction to a patch test with one of the lozenges. Moreover, she recalled that she had had a similar attack of stomatitis on a previous occasion when she had sucked a lozenge of the same brand. The first attack of stomatitis was prior to the use of the hair tonic.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

LYMPHOBLASTOMA IN MICE FOLLOWING ADMINISTRATION OF CARCINOGENIC TAR. AUSTIN M. BRUES and BEULA B. MARBLE, Am. J. Cancer **37**:45 (Sept.) 1939.

In a strain of mice normally exhibiting a 2 per cent incidence of lymphomatosis and a subleukemic blood picture it was observed that lymphoblastoma or lymphatic leukemia developed in 50 per cent of them after the cutaneous application of three different fractions of carcinogenic tars for a prolonged period. The lesions likewise showed a rapid course, whereas the spontaneously appearing lesions were chronic. It was concluded that in the presence of a latent predisposition to lymphoblastoma a carcinogenic agent may act as an extrinsic precipitating factor.

AN EVALUATION OF THE RISK OF BIOPSY IN SQUAMOUS CELL CARCINOMA. RALSTON PATERSON and JOHN R. NUTTALL, Am. J. Cancer **37**:64 (Sept.) 1939.

In a carefully controlled and specially selected group of 166 patients, biopsy specimens were taken from 99 with a sharp ring forceps. The time between the original investigation and treatment and the analysis of the end results varied from one and one-half to four and one-half years, and the lesions studied were from the oral mucous membrane and from the skin. The incidence of metastases was not increased in those histologically studied.

FOERSTER, Milwaukee.

TORULOSIS INVOLVING THE HUMAN CEREBRUM. W. E. ROBERTSON, H. F. ROBERTSON, H. RIGGS and L. SCHWARTZ, J. A. M. A. **113**:482 (Aug. 5) 1939.

A physician aged 61 suffered for four years with attacks of dizziness, syncope, dimness of vision, photophobia and increasing muscular weakness. At times there was incontinence of feces and urine. He experienced increasing memory failure and ultimately complete disorientation. There were hyperreflexia, arteriosclerosis of the fundi and peripheral arteries, tremor of the hands and tongue and muscular atrophy. The eyes showed vertical nystagmoid movements. The leukocytes numbered 17,000 per cubic millimeter, with 92 per cent polymorphonuclear cells. The spinal fluid was not under increased pressure and contained 123 cells per cubic millimeter, of which 50 per cent were polymorphonuclear leukocytes, 44 per cent were lymphocytes and 6 per cent were endothelial cells. Histologic examination of a specimen of muscle ruled out myasthenia gravis. The correct diagnosis was not surmised until the study of postmortem material revealed the organism infiltrating into brain tissue. Part of the symptoms were considered due to the effect of the infection on the cerebral circulation.

HISTOPLASMOSIS OF DARLING. F. J. SHAFFER, J. F. SHAUL and R. H. MITCHELL, J. A. M. A. **113**:484 (Aug. 5) 1939.

A white girl aged 11 months was observed by Shaffer, Shaul and Mitchell because of intermittent fever and vomiting of six months' duration and drowsiness and alternating diarrhea and constipation of one month's duration. The child was suffering with malnutrition and had a rectal temperature of 103.2 F. There was bilateral cervical adenopathy and scaling of the hands and feet. The spleen extended down to the iliac crest, and the liver was palpable 6 cm. below the costal margin. Several tumefactions of purpuric appearance developed and ulcerated. There were leukopenia and anisocytosis. The diagnosis was not established before death. Parasitic bodies were seen in sections of the skin, liver, spleen, pancreas,

intestine, mesenteric lymph nodes, adrenals and bone marrow. The organisms were observed almost without exception in large endothelial cells. By means of the oil immersion technic, each body was found to consist of a central portion surrounded by a capsule. The organism Histoplasma capsulatum was differentiated from Donovan bodies by the irregularity of its chromatin nucleus and because it did not possess a rod. The authors stated that this case of histoplasmosis is the fourth to be reported in the United States and the eighth in medical literature.

DERMATITIS OF THE EAR. H. L. WILLIAMS, H. MONTGOMERY and W. N. POWELL, J. A. M. A. **113**:641 (Aug. 19) 1939.

In a clinical and laboratory study of 25 patients who exhibited eczematous lesions of the external ear, Williams, Montgomery and Powell were unable to establish definitely in any case that the dermatitis was primarily due to a bacteria, fungi or allergy. The pathologic changes observed in 7 of the cases were not diagnostic; they were features suggestive of contact and atopic eczema and of localized neurodermatitis in varying degrees. The bacteriologic observations showed a variety of micro-organisms in the different patients. In 18 of the 25 cases careful removal of detritus and cleansing the external auditory canal were the most important factors in clearing up the dermatitis. No single drug was considered of specific importance; but if a variety of drugs is available, hypersensitive reactions may be avoided, and treatment is usually effective.

A CASE OF PURPURA HAEMORRHAGICA RESULTING FROM SEDORMID. H. H. HUBER, J. A. M. A. **113**:674 (Aug. 19) 1939.

Huber reported the case of a physician in whom systemic reactions and hemorrhagic sequelae developed on two occasions after the ingestion of sedormid (allylisopropylacetylcarbamide). The symptoms began two hours after taking the drug, with a severe chill, followed by fever and later by nausea, vomiting, vertigo and the development of purpuric lesions. During the second attack hemorrhage occurred from the mouth, and the purpuric lesions were numerous. Laboratory tests revealed low platelet counts (dropping to 20,000 per cubic millimeter), a positive result to a capillary fragility test and a bleeding time of over ten minutes. A return to normal conditions followed soon after a blood transfusion.

OCCUPATIONAL LEUKODERMA: PRELIMINARY REPORT. E. A. OLIVER, L. SCHWARTZ and L. H. WARREN, J. A. M. A. **113**:927 (Sept. 2) 1939.

Oliver, Schwartz and Warren report the development of leukoderma in workers who used a particular brand of rubber gloves. The patches of leukoderma occurred on skin under the gloves and in certain instances on covered portions of the body. Patch tests with the chemicals in the gloves showed that an antioxidant caused positive reactions in all the affected workers, and later depigmentation occurred. The trade name of the antioxidant was agerite alba and was said by officials of the company at which the gloves were manufactured to be monobenzyl ether of hydroquinone containing less than 1 per cent of unchanged hydroquinone. When the workers ceased wearing the gloves with the antioxidant, some return of pigment was noted.

EXPERIMENTAL AND CLINICAL GRANULOMA INGUINALE. R. B. GREENBLATT, R. B. DIENST, E. R. PUND and R. TORPIN, J. A. M. A. **113**:1109 (Sept. 16) 1939.

Greenblatt, Dienst, Pund and Torpin coin the word "pseudobubo" to describe the inguinal swelling of granuloma inguinale which they found to simulate the bubo of other venereal diseases. Histologically, the pseudobubo shows the structure of a subcutaneous granuloma. Regional lymph nodes, which were excised and studied microscopically in 4 cases, frequently showed endothelial cells containing Donovan bodies. This showed that the infection may travel by way of

the lymphatics. The condition was experimentally reproduced in 3 human beings and failed to develop in 1. The disease was at its height in about fifty days after inoculation, but the exact incubation period was not determined. The authors failed in attempts to inoculate laboratory animals and were unable to verify the work of others who had previously reported success in culturing Donovan bodies.

INFECTIOUS RELAPSE IN SYPHILIS OF MORE THAN TWO YEARS' DURATION. H. PARISER, J. A. M. A. **113**:1206 (Sept. 23) 1939.

Pariser reexamined a group of 120 patients who had previously received treatment for primary or secondary syphilis and whose infection was of at least two years' duration. He discovered 6 instances of infectious relapse, an incidence of 5 per cent. In 2 of the 6 cases treatment was begun while they were in the primary stage of the disease, with positive serologic reactions. In 4 cases there was a tendency toward early serologic reversal; in 2 of these there was a tendency toward relapse in serologic reactions. While irregularity of treatment is a contributing factor of importance, Pariser states that one is forced to conclude that there exists a small refractory group of patients who in spite of adequate therapy may exhibit infectious relapse.

MASSIVE DOSE CHEMOTHERAPY OF EARLY SYPHILIS BY THE INTRAVENOUS DRIP METHOD. H. T. HYMAN, L. CHARGIN, J. L. RICE and W. LEIFER, J. A. M. A. **113**:1208 (Sept. 23) 1939.

Hyman, Chargin, Rice and Leifer report on the results of treatment in a series of 86 men with primary or early secondary syphilis. The technic of medication followed that used in a preliminary series. The patients were hospitalized, and neoarsphenamine was administered by the intravenous drip method, the average total dose being in excess of 4.1 Gm. The average duration of treatment was slightly less than five days. The results confirm those obtained from the first series. Spirochetes disappeared from the lesions within twenty-four hours, and a reversal of serologic reactions was obtained in 90 per cent of the cases. There were 4 admitted failures, 2 clinical relapses and 2 relapses in serologic reactions. There was 1 death, which was due to hemorrhagic encephalitis. Forty-nine patients (57 per cent) experienced fever early in the course of treatment, and in 54 patients (63 per cent) fever was noted toward the latter part of therapy. Eruptions of scarlatiniform or morbilliform character or simulating erythema multiforme occurred in 42 patients (52 per cent). There was 1 instance of dermatitis exfoliativa. Peripheral neuritis occurred in 31 patients (38 per cent), developing two to three weeks after their discharge from the hospital and lasting as long as four to six months. In 4 patients there developed mild jaundice. An elevated icterus index was noted in 12 patients, but in no instance was there any clinical evidence of hepatic damage. No evidence was found of renal irritation or damage. Besides the fatal case of hemorrhagic encephalitis, 1 patient exhibited a single convulsion, without further symptoms. Nitritoid crises, the various types of atrophy and degeneration of the liver, aplastic anemia and pulmonary embolisms were not present in any case. Approximately 60 per cent of the total administered dose of arsenic was recovered from the urine and feces in 12 unselected cases.

LEWIS, New York.

CUTANEOUS SENSITIZATION STUDIES: II. GROSS AND MICROSCOPIC CHANGES IN RAGWEED AND 2-4 DINITROCHLOROBENZENE SENSITIZATION OF GUINEA PIGS, AND IN POISON IVY SENSITIZATIONS OF HUMAN BEINGS. JULIUS E. GINSBERG, C. DUNCAN STEWART and S. WILLIAM BECKER, J. Invest. Dermat. **2**:81 (June) 1939.

The work of Brunsting and Bailey is repeated in producing cutaneous sensitization to ether extract of short ragweed pollen in guinea pigs through topical applica-

tion of the substance. It is further observed that by continuing to paint the skin of the sensitized pigs, they become desensitized. The analogy of this phenomenon to the "hardening" of the skin of human beings in industry is pointed out. It was found that animals previously sensitized to horse serum showed no greater tendency to become subsequently sensitized to ragweed than did those not so sensitized.

Some of the studies made by Landsteiner and Jacobs on the senitization of animals with simple chemical compounds were also repeated. Animals sensitized to 2, 4-dinitrochlorobenzene by surface application attained the same degree of sensitization as those sensitized by intracutaneous injection of the same substance. Animals sensitized to this chemical showed no greater tendency to become subsequently sensitized to ragweed than did previously unsensitized or horse serum-sensitized animals.

Histologic study of these eczematoid lesions in the guinea pig showed many similarities to those of the human skin. However, there were striking differences, accounted for on the basis of differences in the degree of reaction and on the known differences between human and animal skins. DAVIS, Nashville, Tenn.

ECZEMA MAMMARUM SYMMETRICUM. ROMAN LESZCZYNSKI, Brit. J. Dermat. **51**:301 (July) 1939.

In all of 20 cases of eczema of the nipples and areolas in women the author has also observed dysmenorrhea, that term being used to signify menstrual disturbances in general. This projection onto the mammary skin of an upset in the hormonal or neurovegetative system may be a sensory or trophic reflex which provokes itching and then inflammatory changes. In addition to giving local treatment it is necessary to direct therapy against hormonal disturbances and inflammatory diseases of the genital organs.

THE GLOMUS TUMOR: DOUBTS AND DIFFICULTIES IN DIAGNOSIS. J. H. TWISTON DAVIES, F. F. HELLIER and ROBERT KLABER, Brit. J. Dermat. **51**:312 (July) 1939.

A group of 6 cases is reported in each of which there were reasons for considering a diagnosis of glomus tumor. Masson has described three varieties of glomus tumor: angiomatous, epithelioid (paucivascular) and neuromatous. In addition he has described a "tumeur angio-myome arteriel" and stated the belief that it originates from the glomus. The lesion in 1 of the 6 cases seemed to correspond with this type, and in another it was an example of Recklinghausen's disease with tender angiomatous nodules. In 1 case the lesion was thought to be a heterotopic glomus on the back of the thigh, a site in which the glomus does not normally occur in man. In only 2 of the cases were there typical glomus tumors. The histologic observations are described and illustrated with photomicrographs.

CLASSIFICATION AND DEFINITION OF THE CLINICAL VARIETIES OF ERYTHEMATODES (LUPUS ERYTHEMATOSUS) WITH PARTICULAR REFERENCE TO ITS ACUTE AND SUBACUTE COURSE. ERICH URBACH and CARMEN C. THOMAS, Brit. J. Dermat. **51**:343 (Aug.-Sept.) 1939.

Urbach and Thomas propose a classification of erythematodes (a name which they prefer to lupus erythematosus) that distinguishes chronic, exacerbated and acute forms for both the disseminated and the discoid variety, with a subdivision further into acute and subacute, depending on the duration of the disease. The discoid lesions are characterized by peripheral extension of the borders, and the disseminated ones, by an increase in the number of lesions, rather than by their peripheral growth. With case histories they illustrate the following types of the

disease: (1) chronic discoid, (2) chronic disseminated, (3) exacerbated discoid, both acute and subacute, (4) exacerbated forms of disseminated, both acute and subacute, and (5) acute and subacute forms, depending on duration and constituting the conditions which begin abruptly, without any preceding lesions.

The authors recognize the fact that there may be conditions which overlap and will not permit precise classification. In cases in which there is hypersensitiveness to light and no porphyrin is recovered in the urine or blood, it is suggested that the feces be investigated.

THE USE OF SULPHANILAMIDE IN STREPTOCOCCIC DERMATOSES. JAMES M. FLOOD and JOHN H. STOKES, Brit. J. Dermat. **51**:359 (Aug.-Sept.) 1939.

A group of 6 cases is presented of incapacitating cutaneous eruptions of polyvalent causation, in which hemolytic streptococci played an important role and which with the use of sulfanilamide were brought under control. The conditions were sycosis, dyshydrotic eruptions with secondary infection and various postular dermatoses. After the eruptions were brought under control by sulfanilamide, other treatment was instituted, depending on the cause of the disease.

PERIADENITIS MUCOSA NECROTICA RECURRENS (SUTTON); ULCUS NEUROTICUM MUCOSA ORIS (LOBLOWITZ). A. GIRDWOOD FERGUSSON, Brit. J. Dermat. **51**:366 (Aug.-Sept.) 1939.

Fergusson records a case in which a girl aged 17 had had the disease for five years. The histologic examination showed a nonspecific granuloma, with central necrosis. The literature on the subject is brought down to date.

INFECTION OF A PEACOCK WITH ERYSIPELOTHRIX RHUSIOPATHIAE, FOLLOWED BY A CASE OF HUMAN ERYSIPELOID. AVERIL W. GREENER, Brit. J. Dermat. **51**:372 (Aug.-Sept.) 1939

A case is described in which erysipeloid appeared on the hand of an attendant who handled the carcass of a peacock infected with Erysipelothrix rhusiopathiae.

GOWERS' CASE OF LOCAL PANATROPHY. STANLEY BARNES, Brit. J. Dermat. **51**:377 (Aug.-Sept.) 1939.

The main features of the case were the occurrence of patches in the skin of morphea-like atrophy of irregular distribution and shape. There was no evidence of excessive fibrous tissue in the skin, subcutaneous tissue or muscle, and the morphea-like patches were not bound to the subjacent tissue. The case differs from others described in the literature in that in them there is usually a sclerotic element or a diffuse progressive lipodystrophy. In others the athropy is diffuse, affects large areas and leaves the muscles unaffected.

CHLOR-ACNE IN RAILWAY WORKERS. H. HALDIN DAVIS, Brit. J. Dermat. **51**:380 (Aug.-Sept.) 1939.

An outbreak of chlor-acne in a group of railway workers is reported. The peculiar feature was that only men that worked indoors were affected. They were employed in pulling wire covered with chlorinated naphthalene through conduits which were above their heads. Apparently they were affected when particles of the coating fell on their heads, necks and forearms, for other men engaged in the same work outdoors were not affected. It is thought that outdoors the particles of dust were blown away.

RATTNER, Chicago.

NODULAR CIRCUMSCRIBED GIANT LINCHENIFICATION OF THE SCROTUM. A. TOURAINE and E. LORTAT-JACOB, Bull. Soc. franç. de dermat. et syph. **46**:695 (April) 1939.

The patient, a man aged 42, presented himself for treatment of giant circumscribed lichenification of about a year's duration. There was intense pruritus. On the left side of the scrotum were two large pseudotumors, measuring 30 by 25 cm. and 40 by 25 cm. Under general anesthesia the lesions were excised. Healing was uneventful, and the result was entirely satisfactory, the pruritus being completely relieved.

PRELIMINARY NOTE ON THE USE OF VITAMIN P-P. IN THE TREATMENT OF SEBORRHEA AND ACNE. A. DESAUX, R. GOIFFON and H. PRÉTET, Bull. Soc. franç. de dermat. et syph. **46**:715 (April) 1939.

The authors mention that nicotinic acid seems to influence porphyrin metabolism. They report on acne and seborrhea in 2 young girls, which improved considerably after the administration of nicotinic acid. They merely suggest that their observations encourage further trial of such therapy.

LUPUS ERYTHEMATOSUS. L. M. PAUTRIER, Bull. Soc. franç. de dermat. et syph. **46**:966 (Sept.-Oct.) 1939.

Pautrier recalls that in 1903 he championed the theory that lupus erythematosus is due to the tubercle bacillus. He comments that in the cases in which postmortem examination failed to reveal tuberculosis he always found that some organ had escaped the anatomicopathologic examination necessary for the proof.

Pautrier mentions that in 1926 he expressed his belief that the filtrable forms of the tubercle bacillus plays a role in various so-called tuberculids. He admits, however, that the rarity of positive results of inoculation experiments in lupus erythematosus are discouraging to those who believe in the tuberculous cause, especially in view of the frequency of lupus erythematosus. Even tuberculoid structure is not found, which emphasizes the difficulty in proving that lupus erythematosus is due to the ordinary form of the tubercle bacillus.

He believes that cutaneous tuberculosis must exist in two forms, one due to virulent tubercle bacilli (ordinary type) and the other due to an avirulent or weakly virulent filtrable type, the latter possibly rendered avirulent by the skin itself.

Pautrier also cites Lowenstein's positive results in the blood culture of the tubercle bacillus, admitting, however, that the negative results of other workers were discordant. Pautrier states the belief that some authors in speaking of blood cultures refer to the tubercle bacillus in its classic form, which on culture gives rise to "macrocultures," visible to the naked eye; while others speak of "microcultures," discernible only by scraping the culture plates and staining the debris by the Ziehl method. Certain observers have stated the opinion that organisms forming this type of culture represent the tuberculosis ultravirus, weakly virulent and possessing a low "allergizing" power. The form in which the bacillus circulates in the blood seems to be this young type, giving rise to ultravirusemia. Pautrier believes that the filtrable form of the tubercle bacillus at least offers a good hypothesis as to the causation of lupus erythematosus.

CRITERIA FOR DIAGNOSIS OF LUPUS ERYTHEMATOSUS. H. GOUGEROT, Bull. Soc. franç. de dermat. et syph. **46**:971 (Sept.-Oct.) 1939.

According to Brocq, Besnier and Darier the three main clinical criteria for the diagnosis of lupus erythematosus are erythema, hyperkeratosis (especially follicular) and cicatricial atrophy.

Histologic criteria, as given by Civatte in accordance with Gans, are follicular hyperkeratosis, epidermal atrophy, vascular dilatation, edema of the papillary

body and lymphocytic infiltration, with partial conservation of the elastic tissue in the infiltrate. Civatte also adds lymphocytic exocytosis ordinarily without spongiosis in the epidermis.

Gougerot states the belief that the disease is tuberculous. In 1906 he obtained positive results in 2 cases after inoculation into monkeys. He feels that for successful results large pieces of skin must be used and not merely the fragments obtained during removal of a specimen for biopsy. He cites other observers who have obtained similar successful results (Ehrmann and Reines, Bloch and Fuchs, Cannon and Ornstein, Nicolau and others) and maintains that the efficacy of gold therapy is a point in favor of the theory that lupus erythematosus is a tuberculous disease.

LAYMON, Minneapolis.

STRUMOUS BUBO OF TUBERCULOUS AND LYMPHOGRANULOMATOUS ORIGIN. N. MELZER and K. SIPOS, Acta dermat.-venereol. **20**:135 (March) 1939.

The authors cite a case of a woman presenting a swelling in the inguinal region of one year's duration. The Frei test gave a positive reaction. Pus obtained by puncture was injected into the peritoneal cavity of guinea pigs, in which generalized tuberculosis developed. The patient gave a positive reaction to a Frei antigen made of her own pus (from the bubo). Positive reactions to the same antigen were obtained in 2 other patients suffering from lymphogranuloma. The authors stated the belief that this strumous (scrofulous) bubo was caused by a mixed tuberculous and lymphogranulomatous infection.

CHRONIC LOCALIZED INFLAMMATION CHARACTERIZED BY LYMPHADENOID STRUCTURE. W. L. L. CAROL and J. R. PRAKKEN, Acta dermat.-venereol. **20**:147 (March) 1939.

The authors describe 4 cases of lymphocytomas located, respectively, on the nose, cheeks, ears and labia minora. The histologic picture showed granulation tissue with predominance of lymphocytes.

The literature is reviewed; the clinical manifestations of this entity are described, and the differential diagnosis is considered.

FIVE CASES OF LYMPHOGRANULOMA INGUINALE IN CHILDREN. C. E. SONCK, Acta dermat.-venereol. **20**:171 (March) 1939.

The author describes 5 cases of lymphogranuloma venereum in children whose parents also suffered from the same disease. The girls belonged to three different families, and 3 of them were sisters. Most of the patients and their mothers presented involvement of the rectum with strictures. Three girls also had hydrathroses of the knee joints. The picture of the disease and the course of the infection in small girls does not seem to show any essential difference from that in women. The parents acquired the infection only after all the children were born, which excludes the possibility of the disease's being inherited by the children.

These cases prove that lymphogranuloma venereum can be transmitted not only through sexual intercourse but also in other ways.

TREATMENT OF OCCUPATIONAL DERMATITIS WITH VITAMIN A AND D. I. DAINOW, Acta dermat.-venereol. **20**:191 (March) 1939.

The author describes patients treated with intramuscular injections of vitamins A and D (he used a solution containing 10,000 U. S. P. units of each vitamin in each cubic centimeter). The cutaneous manifestations disappeared, and a real desensitization was obtained. Some of the patients returned to their work soon;

others were treated and cured without having to stop work. The author believes that vitamins A and D exist in the normal skin and that their content in skin varies according to the state of bodily deficiency.

ETIOLOGY OF AURICULAR APPENDAGES. T. BRANDER, Acta dermat.-venereol. **20**:213 (May) 1939.

The author describes a case of a 3 month old girl with bilateral auricular appendages. Her mother and 1 uncle (mother's brother) had the same condition unilaterally. Two other children of the same parents were normal, while a brother of the patient presented the same malformation. Cases are reported in which this condition appeared in only 1 of twins. The author, however, claims to have enough data on families with frequent appearance of auricular appendages to prove to himself beyond doubt that heredity is a decisive factor in the occurrence of these malformations.

SOME PROBLEMS CONCERNING THE PATHOGENESIS OF ALLERGIC ECZEMAS, ELUCIDATED BY EXPERIMENTS ON SENSITIZATION WITH DINITROCHLOROBENZENE. H. HAXTHAUSEN, Acta dermat.-venereol. **20**:257 (May) 1939.

Haxthausen produced a generalized hypersensitivity to 1 per cent solution of dinitrochlorobenzene, by painting a small area of skin once with a 30 per cent solution of dinitrochlorobenzene in acetone. A hematogenous spreading of the hypersensitivity is considered possible, because it appeared on islands of skin isolated from the surrounding skin by means of incisions and with the same intensity as outside the islands. That the epithelial cells are of some importance in the process of sensitization is proved by the fact that freezing with solid carbon dioxide immediately or one to eight days after the painting prevented hypersensitivity in about 80 per cent of the cases. Ultraviolet irradiation one day before the application of the sensitizing solution did not prevent the appearance of hypersensitivity.

PRIMARY TUBERCULOUS INFECTION OF THE SKIN AND MUCOUS MEMBRANE. SVEN HELLERSTKOM, Acta dermat.-venereol. **20**:276 (May) 1939.

The author describes 2 cases of primary tuberculous infection. In a young girl an ulceration on the vulva and inguinal adenitis developed a few weeks after sexual intercourse with a man who had definite tuberculosis of the genitourinary tract. Histologic examination of the ulceration and the lymph gland proved these lesions to be of tuberculous character. The second case was that of a man on whose nose there developed an excoriation due to an accident in a swimming pool. Six weeks later numerous characteristic lupus nodules appeared around the site of the abrasion. The results of histologic examination of a nodule confirmed the diagnosis of tuberculosis.

ASTRACHAN, New York.

Society Transactions

BROOKLYN DERMATOLOGICAL SOCIETY

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November-December 1939

Diffuse Pigmentation, Incontinentia Pigmentia. Presented by Dr. Jacob Skeer.

H. P., a girl aged 14, born in the United States, consulted me because of a generalized pigmentation of four years' duration. The patient stated that it first appeared after sunburn. Both parents are alive and well, and she has a sister, 16 years old, also in good health. As a child she had chickenpox, whooping cough and measles. She complained of headaches about five years ago, but they disappeared after she began to wear glasses. She graduated from elementary school at the age of 13. She began to menstruate at the age of 12 years. Her periods are regular, of six days' duration, with pain the first day.

Physical examination shows that her hair is streaked with numerous gray hairs and that there is slight pityriasis of the scalp. She has a high forehead, prominent bosses and a wide space between her eyes, which are of a mongoloid type. There are numerous pinhead-sized milia on the margins of the upper and lower eyelids and on the malar regions. The posterior cervical glands are somewhat enlarged.

Examination of the skin shows that on the forehead, beginning from the temple region and extending toward the middle, there are irregular, reticulated, blotchy areas of pigmentation, beginning at the hair line and extending to about ½ inch (1.3 cm.) above the eyebrows. The pigmentation branches out and becomes less in the midline. There are a few spots on the malar and mandibular regions and anterior to the ears. The skin of the arms is also involved, especially the external aspect, where there are numerous large patches with many branches, terminating in points in clawlike arrangement, forming irregular circles and segments like the veins of marble. The flexor surfaces and the interior aspects of the arms, as well as the palms, are free of lesions. There are two irregular linear patches in the anterior axillary line. On the back there is a patch over each scapula, with numerous filaments branching out and forming finer projections, terminating abruptly in points. On the extensor surface of both thighs, from the lower third to below the knees and extending on the tibial region of the legs and the calves, there are similar patches. There is decided dermographism. All the finger nails have horizontal linear air spaces, with numerous striations, irregularities and pitting.

The Wassermann reaction of the blood was negative.

Histologic examination showed a positive dopa reaction in the epidermis and only an occasional cell in the corium. Sections stained with hematoxylin and eosin showed that the epidermis and the cutis were practically normal. There were occasional cells containing brownish pigment about the blood vessels and in the corium.

DISCUSSION

Dr. Lesser M. Fruchtbaum: I wonder if this entity should be classified among the nevi. The distribution is in favor of it, and I think that perhaps the histologic examination will confirm this diagnosis.

DR. ABRAHAM WALZER: I think that the clinical description given for incontinentia pigmentia fits well in this case. The picture is that of a bizarre arrangement of irregularly shaped patches of tan pigmentation, with all kinds of peculiarly shaped borders. The final diagnosis rests, I think, on the histologic picture.

DR. JACOB SKEER: Incontinentia pigmentia is a rare cutaneous condition. A study of the histologic sections should give the diagnosis. This condition is supposed to be a congenital ectodermal anomaly which begins in intrauterine life. The anomaly of the ectoderm is often associated with changes of the nails, hair and bones of the skull. The histologic changes chiefly concern melanin. Melanin is found not only in the epidermis but in the cutis, and it is explained by the fact that the basal cells apparently cannot handle the amount of pigment that is formed and it therefore drips into the cutis, producing a sort of tattooing.

Lymphangioma Circumscriptum, Simple and Cavernous. Presented by Dr. E. A. GAUVAIN.

S. B., a boy aged 28 months, is presented from the Methodist Episcopal Hospital. A lesion had been present on the back of the neck for one year. It began as minute, white blisters in an area the size of a nickel. Later some subcutaneous swelling was noted just cephalad to the cutaneous lesion. The swelling increased rapidly to the size of a walnut during the two weeks before presentation.

There is a small group of tense, white or opalescent, pea-sized lesions on the back of the neck, just to the right of the cervical vertebrae. Immediately cephalad to this is a subcutaneous mass the size of a walnut that appears like a lipoma. It is, however, more tense and feels cystic. This tumor mass can be transilluminated.

DISCUSSION

DR. E. A. GAUVAIN: I was interested in the case from the standpoint of the two types of lesions, the simple and the cavernous lesions. As regards treatment, I plan on surgical excision.

A pure angioma could not be transilluminated. The lesion lacks the color of an angioma. Those two points are sufficient to rule out that diagnosis.

Phenolphthalein Eruption. Presented by DR. ARTHUR M. PERSKY.

G. K., a white man aged 69, born in Germany, has lived in the United States for forty-three years. His occupation is that of a bartender. In May 1939 the patient experienced a sudden chill (while walking), followed by an eruption, which he described as itching red patches, involving the entire body except the face. The eruption was diagnosed as "hives." The itching subsided, but in the areas where the red patches were there developed a pigmentation. This persisted until the present except for a few spots which have disappeared. There was no history of drug taking.

Over the lower part of the chest and abdomen are scattered areas, ranging in size from that of a quarter to that of a palm, of reticulated pigmentation enclosing whiter than normal, glistening skin. These areas appear to be atrophic.

DISCUSSION

DR. ARTHUR M. PERSKY: I first saw the patient one week ago today, when he presented a flat pigmented reticulated lesion over the chest and abdomen; the center of the lesion was glistening white. At that time the impression was that the condition might be poikiloderma vasculare atrophicans. I performed a biopsy but was not satisfied with the report. Some physicians thought the condition might be a fixed drug eruption. There was brownish pigmentation at that time, and there was no question of any erythema. He was given three doses of phenolphthalein on three consecutive days and presented himself today with lesions

intensified. The lesions are purplish, violaceous and edematous. The condition is the most acute exacerbation of a fixed eruption due to phenolphthalein that I have observed.

DR. LESSER M. FRUCHTBAUM: I saw this patient four months ago when he presented himself at the Kings County Hospital and took care of him for three months. The lesions were more violaceous then than they are tonight. At that time there was no question that the condition was a phenolphthalein eruption. The patient gave a history of having had a similar attack years ago, and the condition apparently was a fixed eruption. There is no question in this case that it is a typical drug eruption. During these three months the color of the lesions faded to practically pale brown.

DR. M. EDWARD GOEBEL: What is the usual length of time required for a phenolphthalein eruption to disappear after ingestion of the drug is stopped?

DR. SEYMOUR H. SILVERS: I should like to ask whether any one can explain the peculiar color in a phenolphthalein eruption. Has any work been published on this topic?

DR. ABRAHAM WALZER: While cases of multiple sensitivity to drugs are possible, one must also consider that a reaction following the ingestion of one drug may be reproduced nonspecifically by another drug and still that patient need not be sensitive to the second drug. For example, supposing a patient has urticaria from aminopyrine and when that rash has practically subsided the patient takes acetylsalicylic acid. The urticaria may return, not because he is sensitive to acetylsalicylic acid, but because the drug nonspecifically reproduces the eruption. If the patient is given acetylsalicylic acid again a week or two after the original aminopyrine rash has gone, no reaction will occur.

DR. MORTIMER J. CANTOR: There is no question of the diagnosis in this case right now. When I saw the patient originally, one week ago, without the flare-up, the condition looked brownish and reticulated, and, in fact, the white spots looked as though they might be atrophic. One would never think the condition might be a fixed drug eruption, with the peculiar reticulation. The usual type of fixed drug eruption is a discoid patch of pigmentation with infiltration. I think the condition in this case is a rare type of phenolphthalein eruption, simulating poikiloderma.

Erythema ab Igne. Presented by DR. M. EDWARD GOEBEL.

C. B., a woman aged 40, states that about eighteen months ago she applied an ice bag to the right side of her face daily, a few hours a day, for several weeks, because of pain which was caused by a stone in the salivary gland. While she was using the ice bag, the right side of the face became decidedly red and swollen. The redness persisted, in spite of the fact that she stopped using the ice bag. For the last six months this redness has been gradually disappearing.

Examination shows slight atrophy of the skin over the right jaw and some telangiectasia, with a honeycombed brownish pigmentation.

DISCUSSION

DR. DAVID M. DAVIDSON: The eruption in this case consists of a single patch with definite atrophy, telangiectasia and pigmentation. In view of the fact that the eruption is unilateral and not symmetric, as in cases of poikiloderma, and also, in view of the fact that the patient was exposed to roentgen rays for diagnostic purposes, I suggest the diagnosis of roentgen sequelae.

DR. JACOB SKEER: I wonder if the patient applied any tar ointments plus the ice bags, because with all the symptoms that were explained in giving the picture of a roentgen dermatitis, namely, telangiectasia, atrophy and pigmentation, one could readily think of poikiloderma of Civatte. The tissues of the face and chest

simulated an edematous scleroderma. One probably could make a diagnosis of poikiloderma with scleroderma.

DR. DAVID L. SATENSTEIN: I think the diagnosis of poikiloderma is the only possible one to be considered here, for the reasons already given.

DR. ABRAHAM WALZER: This condition is not poikiloderma, nor is it Riehl's melanosis. I would be more inclined to accept it as a reaction to cold applications, as this is not infrequently seen on the abdomen after applications of ice.

DR. G. F. PRICE: Why isn't it possible to get a roentgen dermatitis from exposures at the dentist's office? The output of the x-ray machine may be increased without the dentist knowing about it. About two years ago I had a patient in private practice with a definite roentgen dermatitis from one roentgen ray exposure for an abscessed tooth at a dentist's office. She had a definite roentgen ray burn on the jaw about the size of a quarter.

DR. M. EDWARD GOEBEL: I have seen this woman for the last two months, and it seems to me that the pigmentation is getting more prominent. In view of the fact that it is only on one side and that she had severe redness and swelling when she used the ice pack, I thought the condition was erythema ab igne in an unusual location. Erythema ab igne usually occurs on the abdomen or on the back. This patient is shown because of the unusual location. The term ab igne is used because of the lack of a better one. Atrophy and telangiectasia are also seen with heat and cold burns and sometimes simulate roentgen ray burns. Somehow I do not think that one single roentgen ray exposure for pictures would produce such decided atrophy of the skin or the sequelae that are seen here.

Elephantiasis Nostras. Presented by DR. MAX LERNER.

I. H., a white man aged 30, has been under investigation at the clinic of dermatology and syphilology of the Beth Moses Hospital for about six months. He stated that he injured his left leg about sixteen years ago. An infection developed that incapacitated him for a month, and his left leg and foot became greatly swollen. The size of his left leg and foot has remained stationary.

About five years ago a fungous infection developed in both feet. He received treatment at several clinics.

When seen in August 1939, the patient had active dermatophytosis of both feet, especially the toes, where the eruption was verrucous. This cleared up with local wet dressings.

At present both feet show subsiding dermatophytosis. The left foot and leg are enlarged to about twice the size of the right. The enlargement is due to a solid type of edema, almost fibrotic to the touch. There is little pitting on pressure.

A roentgenogram of the left leg showed no pathologic changes in the bones. The Wassermann reaction was negative. The blood count, examination of the urine and Frei test gave normal results.

DISCUSSION

DR. MORTIMER J. CANTOR: The patient has never been outside of New York. Elephantiasis nostras means that type due to a chronic low grade staphylococcic or streptococcic infection. The condition is more common on the face; there it is known as solid edema. This case falls in the same class. The patient has had no acute recurrences, no fever and no chills. The dermatophytosis which was active is now practically gone, with practically no effect on the elephantiasis.

DR. SEYMOUR H. SILVERS: I treated a patient who had had recurrent acute attacks on the face, which left chronic lymphedema. During the acute stage, I prescribed sulfanilamide. When the acuteness subsided, I treated the patient with fractional doses of roentgen rays. The condition apparently has cleared under this protracted treatment.

Xanthoma Tuberosum Multiplex. Presented by Dr. M. Edward Goebel.

F. L., a seaman aged 59, stated that in 1933 he worked as a watchman and was exposed to the sun, as he did not wear his shirt. Within a short time he noticed a rash on the upper part of his back. The lesions had white tops, and the eruption was itchy. The itching was relieved by baths. However, the eruption persisted, and in 1936, in spite of negative Wassermann reactions, he received sixteen injections of a bismuth compound. The lesions gradually disappeared. In 1938 he underwent an appendectomy, and subsequent to this the eruption reappeared and has gradually become generalized and has persisted. There is no itching at this time.

Examination shows a generalized symmetric involvement of the body, from the neck down, consisting of papules which are discrete and which vary from purple to brown and from chamois colored to skin colored. Some of the papules have a shiny top, and some appear to be umbilicated, as in lichen planus. The liver and spleen are palpable.

The results of chemical examination of the blood were normal. The Wassermann reaction of the blood and the results of urinalysis were negative. The icterus index was 69. Microscopic examination of tissue showed evidence of xanthoma. A roentgenogram of the skull showed mottling of the skull bones, with a bridging across the sella turcica. The long bones were normal.

The patient is shown because of the resemblance of the papules to lichen planus. The diagnosis of xanthoma multiplex was made only after a complete study of the case.

DISCUSSION

Dr. Jacob Skeer: All that I could discern clinically was an eruption of lichen planus. I could not see anything clinically that looked like xanthoma tuberosum multiplex. Some of the lesions showed a yellowish tinge.

Dr. David L. Satenstein: A study of the slides corroborated the diagnosis of xanthoma.

Dr. Mortimer J. Cantor: Clinically, under the artificial light some of the lesions have a peculiar color, not that of lichen planus; but a good many of them have more than the usual papular appearance of lichen planus. They appear dome shaped. Of course this should be better seen in sunlight. They are more elevated and slightly yellowish. There are two to three such lesions on the ulnar aspect of the wrists that are conglomerations of these small xanthomatous masses, which give the clinical appearance of annular lichen planus. I do not know whether the condition should be called xanthoma tuberosum multiplex. It might be better to call it generalized xanthomatosis with peculiar lichenoid lesions.

Dr. Abraham Walzer: This patient has typical lichen planus. He has the papules, arrangement, size, border, central depression and everything that goes with lichen planus. He also has lichen planus lesions of the lip.

Indolent Ulceration of the Leg. Presented by Dr. Abraham Walzer.

H. I., a man aged 19, first appeared at the dermatologic clinic of the Jewish Hospital about a month ago. Outside of a fracture of the skull at the age of 10 years, from which he completely recovered, there was nothing in his past history of any importance. There was no history of tuberculosis in his family. He has always lived in New York.

His present trouble began about a year ago, with an infection of the right palm which had been incised. This was followed by an infection of the left thigh and of the anal region. In May, six months ago, the first "abscess" appeared on the leg, which broke down and formed an ulcer. About three months ago the right leg became similarly involved. Gradually new lesions developed on both legs.

At present he shows about two dozen ulcerations on the legs, more on the left than on the right. The primary lesion is a small pustule, which somewhat

increases in size, breaks and, instead of healing, forms an ulcer which extends peripherally. Thus ulcers of various sizes, shapes and depths are formed, which are indolent and refuse to heal. The edges are irregular and somewhat undermined; some are rolled and have practically no surrounding erythema. The bases of the ulcers are either granular or necrotic. The inguinal glands are not enlarged.

A histologic section of tissue taken from the border showed chronic inflammatory changes. Cultures showed no mycologic organisms but streptococci, diplococci, bacilli and staphylococci. Physical examination, roentgenograms and examinations of the blood and urine showed no abnormalities.

DISCUSSION

DR. LESSER M. FRUCHTBAUM: I, too, had a similar case. A boy voluntarily produced many lesions on his legs. This process went on for a year, until his legs were put in a removable light cast, and then the lesions cleared up. All the lesions in the case just presented are easily accessible. I think the phenomenon is artificially produced.

DR. DAVID M. DAVIDSON: This case is one of extensive pyoderma, regardless of what other name one may wish to call it.

DR. DAVID L. SATENSTEIN: I have observed hundreds of cases like this in the Orient. The condition is common there and usually follows insect bites. Lesions develop which suggest ecthyma and go on to form deep ulcers. Often they are covered by a gelatinous secretion and a thick crust, and when that is removed the lesion is larger than one would expect. The condition is usually due to an infection, but that does not make any difference as far as therapy goes. If the lesions were excised, new ones would appear; the same thing would happen if they were cauterized. I finally packed them with 10 per cent sodium chloride solution, and then the lesions cleared up. That made a poor soil for the organisms to grow. Pyoderma is just a name, and I doubt if the condition in this case is an artefact.

DR. JACOB SKEER: I was able to follow the case. The new lesions began as small red papules, which quickly became pustular and broke down with necrosis and spread peripherally. They are not artefacts.

DR. M. EDWARD GOEBEL: About two years ago I presented a case similar to this one. All the laboratory work showed nothing but staphylococci. More and more lesions developed, and finally there was involvement of the vascular system. Both the legs were amputated, but the patient died. I do not believe the condition is an artefact. I want to emphasize the seriousness of these conditions.

DR. H. H. SAWICKY (by invitation): In Florida among the turpentine workers, where insect bites are common, such ulcerations are not infrequent. They are insect bites, are secondarily infected and are called pseudomycotic infections. Sulfanilamide has been used in these cases, with good results.

DR. ABRAHAM WALZER: The process begins as a pustule and opens, but instead of healing it spreads, forming a round punched-out ulcer. This condition was described by Castellani (ARCH. DERMAT. & SYPH. **18**:857 [Dec.] 1928) under the heading of pseudomycosis. Hamilton (*South. M. J.* **24**:195, 1931) under the title of indolent leg ulcers described the same condition. Various types of organisms have been described, such as organisms resembling gonococci, hemolytic streptococci and others. Under a simple protective dressing of a modified paste, the condition has improved from 50 to 60 per cent.

Pityriasis Rubra Pilaris. Presented by DR. ABRAHAM WALZER for DR. IRVING N. HOLTZMAN.

T. H., a white married man aged 27, an upholsterer by occupation, presented himself at the dermatologic clinic of the Jewish Hospital on Dec. 11, 1939, with

an eruption of eight days' duration. He stated that on the morning of December 3 he awoke with a burning sensation of the skin of his face. Examination in a mirror disclosed a bright redness, with scaling of his entire face. He attributed this to a shaving cream which he had used for the first time the preceding night. However, three days later he noticed a similar redness and "tight feeling" of his hands. This was followed by the appearance of small red "pimples" on his arms, trunk and feet. There was no pruritus.

At present he shows a diffuse erythema of the face, with scaling over the forehead, eyelids and perioral region. This diffuse erythema extends down to the neck line and involves the entire circumference of the neck. Both hands to a point about 2 inches (5 cm.) above the wrists (glovelike) are diffusely reddened, the skin thick and scaling. Pressure on the erythematous area reveals a yellowish discoloration. The arms, trunk and lower extremities present a papular eruption; the individual lesions are pinhead sized and erythematous, some flat topped and lichenoid in appearance and others grayish and conical. These papular lesions are follicular in distribution. On the trunk the lesions impart a grater sensation to touch. In some areas the papular lesions coalesce to form small elevated erythematous patches. The intergluteal area is the site of diffuse erythema surmounted by a coarse, slightly adherent scale.

Histologic examination showed: hyperkeratosis, especially of follicular apertures; slight acanthosis, with intercellular edema of basal and spinocellular layers; slight dilatation of the blood vessels of the corium (subpapillary plexus), and no noticeable cellular infiltrate in the corium or around the blood vessels.

Patch tests with the shaving cream gave negative results.

DISCUSSION

DR. JACOB SKEER: I think the condition has all the symptoms of an acute clearcut pityriasis rubra pilaris.

DR. LESSER M. FRUCHTBAUM: I do not think the condition is as clearcut as was suggested. There are typical lichen planus papules on the body, in the mouth and on the penis. I believe this is lichen planus.

DR. DAVID M. DAVIDSON: The clinical picture here is sufficiently clear to make the diagnosis of pityriasis rubra pilaris. The man presents diffuse hyperkeratosis of both palms and soles and a seborrhea-like eruption on the face. There are numerous keratotic papules at the hair follicles scattered over the body, which coalesce over the elbows, forming patches simulating psoriasis. In my opinion this case has all the features of pityriasis rubra pilaris.

DR. L. J. FRANK: I agree with the diagnosis of pityriasis rubra pilaris.

DR. SEYMOUR H. SILVERS: I agree that this case is one of pityriasis rubra pilaris. However, the patient does not show the follicular keratotic papules on the dorsum of the proximal phalanges.

DR. IRVING N. HOLTZMAN (by invitation): The interesting thing about this case is the extreme suddenness with which the condition began. The patient first presented himself with a bright scaly erythema of the face and hands, and until he disrobed I thought he had a contact dermatitis. The papules first appeared on the arms, and there were also a few scattered ones on the sides of the chest which were red and soft. It was only in this last week that typical follicular papules have appeared.

A Case for Diagnosis (Erythema Elevatum Diutinum?). Presented by DR. ABRAHAM WALZER.

D. R., a clerk aged 39, is presented with an eruption on his face and neck of about four years' duration. There was no history of tuberculosis or other serious illness in the patient or his family.

The first lesions appeared on the back of the neck and behind both ears as itchy red spots, which increased in size and became elevated. They formed either

one patch or a group of nodules. They lasted about three to four months and disappeared, without leaving any marks. New nodules reappeared on other parts of the neck and face and regressed in the same manner.

At present he shows on the back of the neck a number of groups of elevated hard flat nodules, pea sized or a little larger, covered by a thin scale; on the left cheek near the nose is an erythematous slightly elevated round patch, about the size of a quarter, sharply outlined, with a fairly smooth surface and with some telangiectatic vessels running across. There is no suggestion that it might have been made up of a number of individual lesions. On the same cheek at the angle of the jaw is another lesion, semiannular in outline, showing more scaling than the other patch. On diascopic pressure, a faint pigmented area remains. There is no history of ingestion of drugs.

A complete physical examination, as well as examinations of the blood and urine, showed nothing abnormal. Histologic examination of tissue removed from the back of the neck about a year ago showed a subacute inflammatory process, with no features of anything definite.

DISCUSSION

Dr. David M. Davidson: Two forms of erythema elevatum diutinum have been described, the Bury type and the Hutchinson type. The first is supposed to appear over the knuckles in young children, usually girls, and the second type in older persons, predominantly men. However, I do not believe that the eruption in this case simulates any of the types of this disease. To my mind this case is one of lupus erythematosus. Lupus erythematosus which does not leave atrophy has been described, and it can be classified somewhere between the discoid and the acute type. In the future, this condition may become definitely discoid and leave atrophy.

Dr. M. Dickman: The lesions are telangiectatic on the surface, raised and well circumscribed and have no scales. I considered both lupus erythematosus and sarcoid but favor the diagnosis of sarcoid.

Dr. Abraham Walzer: I put that diagnosis down with a question mark because it was the best diagnosis I could make. This disease is of four years' duration, and these lesions come and go. There is little scaling, no patent follicles or any projection of scales in them, and the histologic picture does not show the slightest evidence of lupus erythematosus. The lesions on the back of the neck are nodular and not the type usually seen in lupus erythematosus. There is no clinical or histologic destruction in those lesions. Therefore, I think one also has to question the diagnosis of lupus erythematosus, at least for the present. Regarding the diagnosis of sarcoid, here again one must think of the peculiar development of the lesions and the complete absence of a sarcoid structure. Regarding the question of erythema elevatum diutinum, many of the textbooks still include it under granuloma annulare. I think the condition in this case is the Hutchinson type of erythema elevatum diutinum.

Pseudoxanthoma Elasticum with Angioid Streaks of Retina. Presented by Dr. Seymour H. Silvers.

A. D., an unmarried man aged 43, a resident of the United States for the past seventeen years, complains of generalized itching of two years' duration and of imperfect vision.

Examination shows a well developed man who presents a mild, moist, well defined red macerated eruption in the inguinal region, involving also part of the scrotum. On both sides of the neck, extending to the face and down to the clavicle, there are ill defined patches devoid of hair and having a velvety texture. The color ranges from light yellow to lilac. The follicular openings are evident. Definite papules cannot be felt. The left axilla shows a similar velvety patch about the size of a palm, also devoid of hair but grayish white. A similar patch is present in the right axilla.

A blood count gave normal results except for showing 9 per cent eosinophils. The urinalysis gave normal results. The Wassermann and Kline reactions were negative. Roentgenograms of the bones failed to show Paget's disease. The arteries of the legs showed decided calcification. The histologic examination of a section of skin showed typical pseudoxanthoma elasticum.

DISCUSSION

DR. SEYMOUR H. SILVERS: Since four weeks ago the patient's vision has decreased a great deal. He is a cook and has lost his job because he cannot read the menu. Sometimes when he walks in the street he sees double, and objects appear to him distorted. New hemorrhages are constantly appearing in the eyegrounds.

DR. LESSER M. FRUCHTBAUM: Is pseudoxanthoma elasticum always associated with ocular symptoms?

DR. SEYMOUR H. SILVERS: In a great number of cases there are associated ocular symptoms. Extensive roentgenograms of the skull and long bones did not reveal anything abnormal in this patient.

Multiple Idiopathic Hemorrhagic Sarcoma (Kaposi). Presented by DR. C. B. LOCASTO for DR. E. A. GAUVAIN.

W. B., a white man aged 73, is presented from the Kings County Hospital. He states that he has had bluish red, slightly infiltrated plaques on the dorsa of both feet for twenty years. Five years ago he received twelve roentgen ray treatments during three weeks, without any evident improvement in the lesions. He has also had diabetes for twenty years and has recently been receiving 20 to 30 units of insulin daily.

On the lateral and dorsal aspects of both feet and extending up the outer side of the left leg are bluish red, slightly elevated plaques with sharp borders. There are also several pea-sized to dime-sized lesions of a similar nature on the legs. On the dorsum of the left foot, in the center of one of the plaques, is a pea-sized vascular tumor resembling a granuloma pyogenicum.

Examination of the blood showed 177 mg. of sugar per hundred cubic centimeters, with no other abnormalities. Examination of the urine showed a 2 to 4 plus reaction for sugar and a faint trace of albumin. The histologic diagnosis was multiple idiopathic hemorrhagic sarcoma (Kaposi).

DISCUSSION

DR. ARTHUR M. PERSKY: There is no question in my mind as far as the diagnosis is concerned, but the patient was brought here because after he was kept in bed for twenty-four hours the lesion blanched so considerably that the diagnosis of Kaposi's sarcoma could not be made. If the condition were Kaposi's sarcoma, would the lesion blanch when the leg is elevated?

DR. DAVID M. DAVIDSON: Last year I presented before this society (ARCH. DERMAT. & SYPH. **39**:1081 [June] 1939) an old man with Kaposi's sarcoma who showed besides the more characteristic lesions on the legs, the same flat, almost nonelevated, red, violaceous patches as this patient presents tonight. The fact that the erythema becomes paler when the patient is lying down can be explained by the fact that the condition is here in the inflammatory-angiomatous stage, and while he is lying down the blood drains out of the vessels.

DR. ARTHUR M. PERSKY: I might add that about one week ago the patient had a pea-sized granulomatous mass on the dorsum of the foot which was thought to be a pyogenic granuloma.

Lichen Planopilaris (Pringle). Presented by DR. LESSER M. FRUCHTBAUM.

H. P., a man aged 56, presented himself on Nov. 18, 1939, at the Unity Hospital, with a history of having had a rash on his body and scalp for four weeks. The Wassermann test performed during that period gave a negative reaction.

The patient presents a generalized, profuse, somewhat pruritic eruption over the anterior and posterior aspects of the entire trunk and on the anterior aspect of the upper portion of both thighs. A few lesions are also present on the upper extremities, the forehead and the vertex of the scalp. There are no lesions on the forearms or penis. On the trunk the lesions are a mixture of flat, polygonal, violaceous papules and conical papules surmounted by thorny spines.

DISCUSSION

DR. DAVID M. DAVIDSON: As this patient presents lesions of lichen planus and lichen spinulosis on the body and lesions resembling pseudopelade on the scalp, I should say that this is a case of Little's disease. I believe that Feldman described the pathologic changes of these lesions, all of which are supposed to show the typical picture of lichen planus.

DR. SEYMOUR H. SILVERS: This is a rare disease. I should like to hear from those who have had an opportunity to observe other similar cases.

DR. LESSER M. FRUCHTBAUM: The atrophy on the scalp is not a result of these lesions but is due to a burn which involved the entire scalp and which was present before the development of the lesions. I made the diagnosis of lichen planopilaris owing to the coexistence of the two types of lesions. On the scalp the lesions are almost macular; on the rest of the body they are papular.

The picture has changed since one month ago. At that time the lesions on the scalp were violaceous, whereas now they are more brownish. Only a few typical lichen planus lesions are evident on the anterior aspect of the upper portion of the thighs. All the lesions have gradually developed into the flat-topped, shiny, polygonal papules of lichen planus. There is no atrophy of the skin.

A Case for Diagnosis (Dermatophytid?). Presented by DR. LESSER M. FRUCHTBAUM.

E. B., a man aged 55, presented himself at the Long Island College Hospital about a year ago, with a generalized eruption on the trunk. Prior to that he was hospitalized with the same condition for several months. The lesions first appeared on the forearms and then spread to the trunk and lower extremities. They arose in crops, remained for several weeks and then cleared up. At no time was he entirely free from lesions.

The lesions now are mostly discrete and round, with clearing centers and infiltrated borders, and are topped with scales. On the forearms and hands the lesions have the appearance of eczematous dermatitis.

Intradermal tests revealed sensitivity to house dust. Desensitization with house dust, however, did not clear up the condition. Laboratory tests, including biopsy, gave negative results.

DISCUSSION

DR. M. EDWARD GOEBEL: This man was seen by me about two to three years ago. Prior to that he was also treated by Dr. Graham, and he also attended the clinic at the New York Post-Graduate Medical School and Hospital. He had a generalized eruption at the time, consisting of erythema, vesicles and crusting, which presented the appearance of a contact dermatitis. A similar diagnosis was made at the New York Post-Graduate Medical School and Hospital clinic and also by Dr. Graham. His condition when seen by me was so severe that he had to be hospitalized, and he remained in the hospital about three months. However, since that time he has had periods in which his skin was clear and periods in which a dermatitis occurred. Urticarial wheals were also associated with the dermatitis. Laboratory tests at the time, including blood counts, urinalyses and Wassermann tests of the blood, gave negative results. Microscopic study of the skin showed a dermatitis. The patient used only paper and pencil at work and did nothing at home to account for the dermatitis. The

rash is different now from what it was when first seen two or three years ago. This is the first time I have had an opportunity of seeing him in five months. The picture is now one of mycosis fungoides.

DR. J. C. GRAHAM: I saw this patient when his cutaneous lesions first began and at that time made the diagnosis of a contact dermatitis. However, I was unable to locate the causative factor. I agree with Dr. Goebel's statements about him.

DR. DAVID M. DAVIDSON: I do not believe that a dermatophytid ever produces such lesions. The condition might possibly be a toxic eruption due to some drug, but on account of the bizarre forms that these infiltrated patches produce, I am more inclined to suggest the diagnosis of mycosis fungoides.

DR. L. J. FRANK: To me the lesions looked round and infiltrated, and on the lower part of the body they seemed more like erythema multiforme lesions. There was central clearing but not the central clearing one sees in dermatophytids. The lesions were acute, those on the arms being slightly infiltrated. The condition in this case should be considered as a premycotic stage of mycosis fungoides but not one of dermatophytid.

DR. H. L. FEIGENBAUM: This is an unusual case, in that it presents certain features of many different types of cutaneous diseases. There are some psoriatic lesions, especially around the scalp and hair line on the back of the neck. There are also some plaques on the forearms that have a psoriatic appearance. On the posterior part of the thighs the configuration of the lesions and their color are those of erythema multiforme. There are no lesions suggestive of dermatophytid. I, too, should be inclined to call the case one of mycosis fungoides, in the early, or pretumor, stage.

DR. ABRAHAM WALZER: The first impression that one gets is that the case is one of mycosis fungoides, but the color is somewhat against that diagnosis, being too red. There is a peculiar configuration of the lesions, which are indurated and infiltrated. Furthermore, these lesions are evanescent. The condition cannot be a contact dermatitis because of the peculiar type of lesions. I believe that it might be toxic annular erythema with some edema. There is one other possibility and that is an annular edematous type of Duhring's disease, in which there are recurrent attacks of annular edematous erythema.

DR. LESSER M. FRUCHTBAUM: It was interesting to hear all the diagnoses suggested—dermatitis venenata, mycosis fungoides, erythema multiforme and dermatophytid, which was my last diagnosis with a question mark. When the patient consulted me a year ago there were typical lesions of mycosis fungoides, not the type seen tonight but infiltrated lesions with raised borders and no scaling of any kind. The lesions would disappear and reappear. The eruption reappeared one month ago. Tonight the picture varies from the one presented two weeks ago. Up to that time several eczematous lesions were present on the neck, in the groins and on the dorsum of the hands that were typical of dermatophytosis, especially those in the groins.

This man suffers from intense itching. When the lesions clear up he is perfectly well, and when they reappear he goes through the various stages again. He does not present the clinical picture of mycosis fungoides. That diagnosis can also be excluded by the history. Several biopsies were performed, and none revealed the picture of mycosis fungoides. In connection with the possibility of erythema multiforme, I tried to locate the focus of infection, without success. The patient was sensitive to house dust by scratch test. There were numerous lesions on his toes which clinically looked like dermatophytosis, which suggested that the lesion was a dermatophytid.

Tuberculosis of the Skin. Presented by DR. G. F. PRICE.

J. C., aged 8 years, born in this country, is presented from the dermatologic clinic of St. Mary's Hospital. He had pneumonia in December 1937, followed by an ulceration on the outer aspect of the right ankle, which took about eight

months to heal. He had pneumonia in December 1938, followed by an ulceration on the lower third of the left leg. Both areas healed with an atrophic scar, studded with islands of normal tissue.

The condition began about October 1 as an acute inflammatory process, simulating a cellulitis. A smaller lesion on the left thigh began at the same time but responded to ammoniated mercury ointment U. S. P. The present lesion rapidly grew to its present size and proceeded to break down, discharging a thin, pale watery purulent discharge in three different areas. The patient was put to bed and given a high caloric diet, and with the use of ammoniated mercury ointment and sterile petrolatum the two upper ulcers healed. The lower ulcer is still open but reduced to about one-third its actual size.

The Wassermann reactions in October and November 1939 were negative. The urine was normal. Examination of the blood showed: 9,500 white blood cells and 4,630,000 red blood cells per cubic millimeter and 86 per cent hemoglobin, with a differential count of 74 per cent neutrophils, 1 per cent eosinophils and 25 per cent lymphocytes. A smear showed no organisms. A culture showed gram-negative bacilli. A subculture was not identified (probably a contaminant). Microscopic examination on November 30 showed tuberculosis of the skin.

MANHATTAN DERMATOLOGIC SOCIETY

GEORGE C. ANDREWS, M.D., *President*

ANTHONY C. CIPOLLARO, M.D., *Secretary*

Dec. 12, 1939

Cheilitis. Presented by DR. GEORGE M. LEWIS.

G. B., a college student aged 25, is presented from the Skin and Cancer Units of the New York Post-Graduate Medical School and Hospital. Inflammation of his lower lip developed eight months ago. Investigation in California and in New York did not reveal any contact, such as with toothpaste or lipstick, which could account for the eruption. He had eleven fractional (75 r) exposures to unfiltered roentgen rays at weekly intervals, various types of local therapy and restricted diets, to eliminate possible food allergens. Cultures failed to demonstrate any pathogenic fungi.

The patient presents acute inflammation of the lower lip, with redness, vesiculation and profuse scaling. Many of the vesicles have ruptured. The upper lip is similarly involved but to a less severe degree. Palpation confirms the fact that the inflammation is superficial.

DISCUSSION

DR. DAVID L. SATENSTEIN: The causative agent might be sunlight. I have seen similar conditions occurring during the summer, especially in persons who go to the beach and expose themselves a good deal. They get this type of lesion, and it persists for a long time. Such conditions are difficult to clear up. I have a patient coming to the office now whose eruption began in the early part of the summer. She is a young girl who went to the beach to tan. Her lip became swollen, and the vesicle formed. Every time she gets in the wind her lip swells. I therefore suggest sunlight as a possible cause. As a test I would expose the patient to a small amount of ultraviolet radiation.

DR. HOWARD FOX: Cases of cheilitis exfoliativa have usually presented two difficulties for me: I have seldom been able to discover the causation, and I have rarely been able to get beneficial results from treatment. Cosmetics, dentifrices and sunlight play a part in some cases.

DR. ANTHONY C. CIPOLLARO: I should like to ask if the manifestation of neurodermatitis ever resemble cheilitis.

DR. E. WILLIAM ABRAMOWITZ: The consensus among nutrition experts is that there is a deficiency of vitamin B in the diet of the general public. I suggest the administration of riboflavin, in view of its favorable action against cheilitis of obscure origin.

DR. PAUL GROSS (by invitation): If contact dermatitis can be ruled out in this case, two other possibilities remain. One was mentioned by Dr. Abramowitz. Yet I do not believe that the cheilitis of this patient fits in with the picture of riboflavin deficiency, as described by Sebrell and Butler. Notwithstanding, a therapeutic test with riboflavin seems justified. The other condition to be considered is that of an exfoliative cheilitis confined to the lower lip, which really is a precancerosis. Microscopic examination may show changes of the epidermis, suggesting the latter diagnosis.

DR. MAX SCHEER: I think in this case the causative factor is probably exposure to light. The condition began when the patient was in southern California, and it was always most intense when he resided in that region. Having once begun, the condition persisted.

DR. GEORGE C. ANDREWS: If light sensitization were the important factor, one would not expect involvement of only the upper lip.

DR. GEORGE M. LEWIS: This man's case has been thoroughly studied from the standpoint of cosmetics and all possible external sensitizers with the exception of light. He will be further studied for the possibility that vitamin B deficiency is responsible or that the condition is a form of neurodermatitis or a manifestation of neurasthenia. If precancerosis is a possibility, the question of a biopsy must be kept in mind. There is a history of seborrhea, but his scalp has been free of that disorder since he has been in New York.

Mycetoma. Presented by DR. GEORGE M. LEWIS and DR. WILBERT SACHS.

A. N., a white man aged 64, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. He fell and scraped his right hand on a wooden floor ten years ago. A number of splinters were removed, and later incisions were made over several fluctuant areas, with evacuation of pus. Since then there have been periodic swellings, many of which have opened spontaneously. Dark granules, of various sizes and having resemblance to foreign bodies, were frequently noted in the pus. A microscopic examination shortly after the onset showed a foreign body reaction in the tissues. Three months before admission, after striking his hand, swelling of both the palm and the back of the hand occurred.

Examination reveals many sinus tracts in the palm, from which pus can be expressed. The pus contains many dark granules varying in size from that of the head of a pin to that of a split pea. The granules are irregular and for the most part angular. The back of the hand shows several subcutaneous swellings, which are firm, movable and not attached to the skin. No sinus tracts lead from these swellings.

Microscopic examination of the granules showed a rather coarse mycelium. A cultural growth was obtained with difficulty; the fungus was probably a species of hormodendron. Histologic studies showed the black granules in the tissues from specimens of the palmar lesions and of a deep subcutaneous nodule on the back of the hand. Roentgen studies showed the bones to be unaffected in the disease process. The Wassermann reaction of the blood was negative. A complete blood count and a urinalysis revealed no abnormalities.

DISCUSSION

DR. GEORGE M. MACKEE: I agree with the diagnosis of deep fungous infection because of the microscopic demonstration of mycelium, and I accept the diagnosis of mycetoma, because it was made by a good mycologist.

DR. WILBERT SACHS: When I saw this patient, the first thing that was apparent was the clublike appearance of the extremity. I saw the patient reported

on by Drs. Gammel, Miskdjian and Thatcher (ARCH. DERMAT & SYPH. **13:** 66 [Jan.] 1926) and though the lesion was on the foot the same feature was striking. In this patient, besides the clublike appearance of the hand, there were many vesicular lesions, some containing black granules and others yellow. With these features, the diagnosis of mycetoma was suggested. If the lesions were on the foot instead of the hand, I believe the diagnosis would be much more evident. Cases of mycetoma of the hand have been reported in the literature (Pels, I. R.: *J. Cutan. Dis.* **37:** 740, 1919).

DR. E. WILLIAM ABRAMOWITZ: I have observed only 1 such case before, and in that the lesion was on the foot of a Negro. I am interested to know what treatment, if any, is effective.

DR. WILBERT SACHS: Regarding treatment, the books recommend iodides and at times amputation. Dr. Cole's patient was hospitalized for a long time, and even with all types of therapy, improvement was not noticeable.

DR. ANTHONY C. CIPOLLARO: I should think this would be a favorable opportunity to give ethyl iodide inhalations. If the inhalations are carefully given, I do not believe that this form of therapy would be dangerous, even if used for elderly patients.

DR. GEORGE M. LEWIS: The granules are protected by a hard capsule, and this has to be pierced before medication can be effective. At present we are administering iodides intensively. Amputation is sometimes necessary if there is involvement of bones. We have not yet definitely classified the micro-organism.

Dermatitis Herpetiformis Treated Successfully with Sulfapyridine. Presented by DR. MAURICE J. COSTELLO.

A. C., an unmarried woman aged 22, was presented before this society on May 9, 1939 (ARCH. DERMAT. & SYPH. **41:**134 [Jan.] 1940). In April 1939 she was given 7½ grains (0.48 Gm.) of sulfapyridine three times a day for one week and then twice a day for the following week. The eruption, which was unusually severe, completely disappeared in about three weeks. There has been no recurrence. The areas of localized residual pigmentation and superficial scarring persist.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: I presented before the class at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital a patient with dermatitis herpetiformis who showed great improvement after taking sulfanilamide. I tried giving it in 2 other cases, with similar results. It is not necessary to order the large doses that are being used for severe systemic conditions. I have not used sulfapyridine. It is hoped that no recurrences will develop when administration of the drug is discontinued.

DR. GEORGE M. MACKEE: In my experience, sulfanilamide and sulfapyridine in dermatology have been uncertain drugs. One sees occasional good temporary results in pemphigus, erythema multiforme, lupus erythematosus, acne varioliformis, sycosis, vulgaris, dermatitis herpetiformis and even acne vulgaris, but failure is common. They are used because sometimes the results are satisfactory. Some people can take these drugs with no unfavorable reaction, while others cannot.

DR. HOWARD FOX: I saw this patient with Dr. Costello when she presented a typical picture of Duhring's disease of five years' duration. Shortly after treatment with sulfapyridine new lesions ceased to appear, and the condition has not recurred for the past eight months. The result was striking, and I think sulfapyridine merits a trial in other cases of this rebellious disease.

DR. MAURICE J. COSTELLO: I agree with Dr. Fox that there was relief of itching and remarkable improvement in this patient's eruption within three days after the initial dose of sulfapyridine. In two weeks there was complete disappearance of all the active lesions, and itching was absent. It is interesting to note that the patient has remained free of the eruption in spite of the fact that

administration of the drug has been discontinued now for seven months. The residual hyperpigmetation in localized areas bears evidence of the severity of the eruption, which had been present for five years.

Lichen Planus, Severely Excoriated. Presented by DR. MAURICE J. COSTELLO.

A. S., a woman aged 62, was born in Germany. She is of nervous temperament. She had an appendectomy five years ago and excision of a lipoma four years ago. The duration of the present eruption is two years. It has become worse in the past month. It appeared first on the flexor aspects of the wrists and the inner aspects of the thighs.

The eruption she now presents is generalized except that there are no lesions on the face and neck. The interesting feature of this eruption is severely excoriated lesions resembling those of pediculosis corporis. In several areas can be seen the typical, shiny, umbilicated, flat papules of this disease. The oral lesions are characteristic. The Köbner phenomenon is present.

DISCUSSION

DR. HOWARD FOX: Lichen planus resembles pityriasis rosea in one respect: In some cases there is moderate itching; in others the itching is severe, and in some there is no itching at all—at least, in the average case of lichen planus one does not see many scratch marks. The case presented today happens to be one in which the skin has been severely excoriated.

Melanocarcinoma. Presented by DR. MAURICE J. COSTELLO.

A. T., a man aged 23, was presented before this society a year ago (ARCH. DERMAT. & SYPH. **40**:298 [Aug.] 1939). He is presented this evening to show that his course since then has been favorable. His weight has been normal, and he is without symptoms. Examination does not disclose any new lesions or metastases to the neighboring lymph glands.

Treatment has consisted of irradiation with radium of the lower half of the left ear and the preauricular and postauricular regions, as well as the regional cervical and axillary lymphatic glands. In addition to the malignant melanoma lesion, which is smaller than it was last year, he has a mild radium dermatitis.

Melanocarcinoma Following the Treatment of a Common Mole. Presented by DR. MAURICE J. COSTELLO.

A. S., a white girl aged 18, presented herself on April 14, 1936, when she was 14 years old, for treatment of a pigmented, dark brown, hairy common mole, measuring 1¾ by 1½ inches (4.45 by 3.8 cm.) and located on the left side of the nose. There had been no increase in size or in pigmentation prior to this time. She wished to have it removed because it was a cosmetic deformity. Its size and location made complete surgical excision inadvisable. The lesion was treated by electrodesiccation on April 21, May 5, June 16 and July 7, 1936. On July 14, July 28 and September 15 it was treated by the application of solid carbon dioxide for ten to fifteen seconds, with moderate pressure. The patient was observed on March 25, 1937. The cosmetic result was good. The treated area was light red.

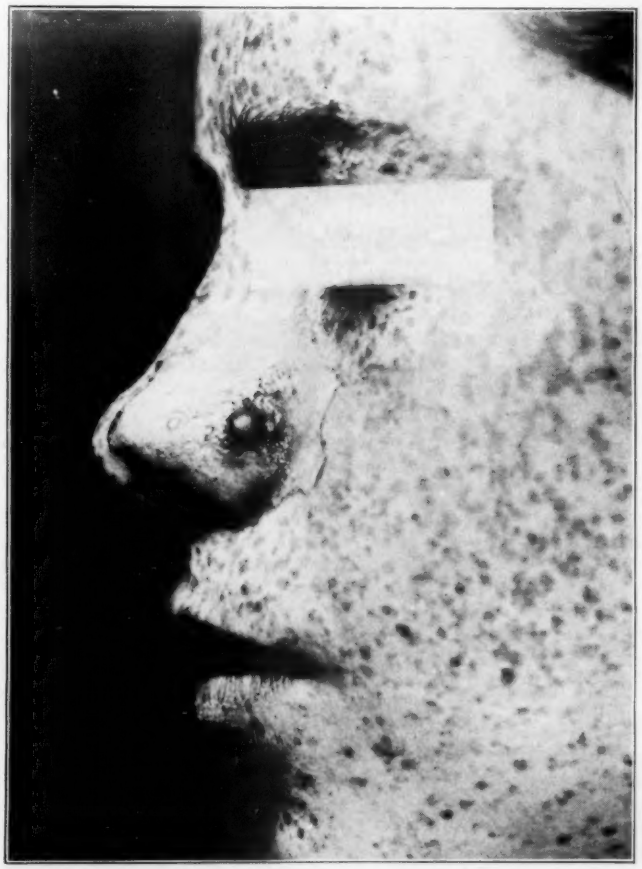
On April 27 in the center of the aforementioned site was a rounded pea-sized, blue-black lesion, which the patient claimed appeared two weeks previously. A clinical diagnosis of malignant melanoma was made, and because of delay in the biopsy report the lesion was irradiated with radium. It received 500 milligram hours, and the regional cervical lymphatic glands, 12,000 milligram hours.

She was examined on July 12, 1937. The wound inflicted during removal of tissue for biopsy had healed, and melanotic pigment was scattered through the surrounding skin. The report of the histologic examination by a general pathologist showed "an irregular hyperplastic, well differentiated, stratified squamous epithelium, with long coarse papillae and an underlying derma of dense hyaline fibrous tissue, which supports a moderate number of large uniform nevus cells

and a great number of deeply pigmented chromatophores." The diagnosis was "pigmentary nevus."

Roentgenograms of the lungs, bony thorax and osseous part of the nose were normal.

The patient was not seen again until November 1939. In the interim, she enjoyed good health, and the lesion on her nose had changed little. There were



The area enclosed by the ink line is the former site of a common mole. The melanocarcinoma in the center appeared one year after treatment.

increased punctate and pinhead-sized bluish black satellites surrounding the pea-sized solid lesion. A careful examination revealed no new pigmented lesions on her body, although, as the photograph shows, she had numerous dark brown freckles which had been present since early childhood.

The appearance of the lesion, which had not changed, suggested a reexamination of the histologic specimen. Dr. Symmers, Dr. Johanssen and two dermatopathologists, Dr. Satenstein and Dr. Sachs, concurred in the histologic diagnosis of melanocarcinoma.

DISCUSSION

DR. GEORGE M. MACKEE: This patient interests me because of the fact that the original diagnosis was common hairy pigmented mole. I do not believe that

the original diagnosis was correct. All physicians have different conceptions about just what is meant by the term "common mole," which, incidentally, is a poor designation. I personally have never seen malignancy following what I call a common mole. I think the lesion was a benign melanoma which became a malignant melanoma. It is not rare to have roentgen rays or radium in large doses delay the process or make it quiescent or, on occasions, effect a cure. However, this lesion is not cured. It is still present, and I should think, for the protection of this patient's future, that it would be well to institute surgical treatment.

Dr. Anthony C. Cipollaro: I should like to confirm what Dr. MacKee said. Statements are frequently made that malignant melanomas arise from ordinary common moles. This is contrary to the experience of many of the older dermatologists who have had many opportunities to observe many patients after treatment with various methods.

Dr. E. William Abramowitz: When a patient presents himself with a brown, elevated, pigmented mole with no hair growing in it, I never feel certain that it is absolutely safe for me to go ahead and remove it, except surgically. But when it is on the face of a woman, I always feel that the responsibility should be shared by having another opinion before any procedure is undertaken. The French dermatologists say that this type of lesion can be treated safely with electrolysis.

Dr. David Bloom: I have observed the patient from the start, and I recall the nevus as an infiltrated plaque on the lower part of the left side of the nose, dark brown and having fuzzy hair. It was not the usual circumscribed, pigmented, hairy nevus which is seen frequently and which one does not hesitate to treat. This case has impressed me so that in the future I shall look on such plaques as potentially malignant or at least give a guarded prognosis.

Dr. Paul E. Bechet: The question as to the advisability of removing pigmented moles comes up with definite regularity at many dermatologic meetings and probably will continue to do so in the distant future. Personally, I am guided by the color and number of moles present. In the presence of dark, elevated, bluish black nevi, either single or multiple, or when there are dozens of nonhairy moles on the face and even on the body, I prefer not to intervene. On the other hand, I have, over the space of many years, removed hundreds of pigmented moles, both hairy or nonhairy, without noting a single instance of subsequent malignancy. I believe that the development of malignant tissue after the removal of a pigmented mole can be greatly obviated by thoroughness in its removal. Most of the disastrous results that I have noted apparently followed inadequate removal and inappropriate technic. Squeezing, scratching and picking moles are not uncommon habits even among intelligent women and are also important causative factors in malignant change. I have so frequently listened to a discussion of the subsequent dangers of intervention and so seldom observed them that I am greatly inclined to believe that physicians suffer too much from the fear of malignancy. Dr. Costello's case, however, proves that in rare instances this fear is not entirely unwarranted.

Dr. Wilbert Sachs: It is quite possible that the original diagnosis as well as the one presented tonight are both correct. It is not uncommon to find a combination of nevi in a single specimen. This patient may have a junction type nevus in combination with one of the other types of epithelial nevi.

After looking at the slide, it is gratifying to see that this patient is not only alive but apparently in good health. The microscopic picture is that of a nevocarcinoma.

Dr. Howard Fox: I recall when the girl was first presented at our weekly conference at Bellevue Hospital as having an ordinary pigmented and hairy nevus of the side of the nose. At that time the hair covering the nevus was definitely profuse and long. Orders were given to treat her with solid carbon dioxide or by electrodesiccation. When I saw her later, I was shocked to see a lesion that was clinically a nevocarcinoma. This was the first time I had seen a malignant

growth develop after proper treatment of an ordinary pigmented and hairy nevus. I consider this a unique case.

DR. DAVID L. SATENSTEIN: I have not seen any, read any or heard of any reports of a cutis type nevus eventuating in a malignant growth. Here is a case of a nevus that supposedly turned out to be a junction type. It was a junction type from the start, taking the clinical picture of a common mole in the beginning. These mistakes have been made often, but our attention has not been called to them.

DR. MAURICE J. COSTELLO: This patient had been seen by the members of the Dermatologic Staff at Bellevue Hospital before the original lesion was treated, and the consensus of those present was that the patient had a pigmented, dark brown, hairy mole. The same group agreed that the blue-black, pea-sized, elevated nodule which appeared one year after treatment of this mole was clinically a malignant melanoma, and the diagnosis was confirmed by histologic study.

Parapsoriasis Varioliformis. Presented by DR. MAURICE J. COSTELLO.

H. C., a married laborer aged 26, has had an eruption almost continuously for twenty years. No member of his family is similarly affected.

The patient presents a chronic, generalized, extensive eruption, consisting of flat and scaly papular lesions resembling both pityriasis rosea and lichen planus. He also has a number of vesicles and papulovesicles. There are vesicular lesions in the mouth on the buccal mucosae, the hard and soft palates, the tongue and the lips. The glans penis is occasionally similarly affected. Scaly, flat papular lesions are seen on the scalp, palms and soles. There are a number of punched-out and irregular lentil-sized cicatrices on his face.

A histologic examination confirmed the diagnosis of parapsoriasis varioliformis.

His Wassermann reaction was negative. He had gonorrhea in 1934.

His treatment has consisted of intravenous injections of typhoid vaccine in graduated doses, solution of potassium arsenite U. S. P. and various salves and lotions, as well as ultraviolet irradiation.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: I think that this case is one of parapsoriasis, but I am not certain that the condition is the varioliform type.

DR. PAUL GROSS: The condition is chronic parapsoriasis with occasionally pure varioliform lesions. It is this type of eruption that forms a link between the chronic and the acute varioliform parapsoriasis. Another lesion found in both varieties is the small lichenoid flesh-colored papule, which was described by Wallhauser many years ago.

DR. MAURICE J. COSTELLO: I have observed this patient for about seven months. The lesions of this polymorphous eruption resemble pityriasis rosea and lichen planus, while other lesions are vesicular. During the periods of exacerbation the vesicular element predominates. The patient claims that up to the present time ultraviolet irradiation has given him the greatest relief.

GEORGE C. ANDREWS, M.D., *President*

ANTHONY C. CIPOLLARO, M.D., *Secretary*

Jan. 9, 1940

Lichen Planus Followed by Lichen Pilaris (Vitamin A Deficiency?). Presented by DR. E. WILLIAM ABRAMOWITZ.

Mrs. T. B., aged 32, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. Typical lesions of lichen planus

developed about four months ago. The eruption was generalized, and she had considerable itching. The patient received injections of sodium arsenate and roentgen ray therapy, the latter being applied not only to the affected areas but to the spine.

After one month of treatment, grouped lichen pilaris lesions began to appear on different parts of her body, and also some pigmented elevated tags became noticeable on her neck and trunk. The administration of sodium arsenate was then discontinued. She never had any lesions in her mouth.

The patient has been eating only one meal a day.

The diagnosis is lichen planus followed by lichen pilaris or cutaneous lesions due to vitamin A deficiency.

DISCUSSION

DR. HOWARD FOX: I think it is possible that this eruption is due to vitamin A deficiency and suggest that the patient be tested for night blindness.

DR. MAX SCHEER: I think that the keratosis pilaris is due to avitaminosis. I questioned her as to the contents of her one meal a day. She stated that she ate little or no butter, and there was almost a complete absence of vitamin A in her diet. Furthermore, the distribution of the lesions, for example on the forearms and trunk, are in favor of vitamin A deficiency in this case.

DR. ISADORE ROSEN: I should not associate this generalized lichen-pilaris-like eruption with a vitamin deficiency. In view of the fact that this patient has had therapy which included arsenic sufficient to influence the extensive lichen planus, I should be inclined to associate the present eruption with the arsenic that she has received.

DR. MAX SCHEER: The patient stated that her diet included oils, fats, vegetables and meat. The oils, like olive oil and salad oil, contain at the most only faint traces of vitamin A. There is none in meat and practically none in the vegetables that she eats. The only sources from which she could get it are eggs, butter and milk, mainly butter, and she does not eat any butter.

DR. MAURICE J. COSTELLO: Patients are occasionally seen at Bellevue Hospital with keratotic papular lesions similar to those in this case, and I have never obtained a history of inadequate vitamin intake. This afternoon I saw 2 brothers, 7 and 9 years of age, 1 of whom had an eruption which clinically resembled those which have been described as due to vitamin A deficiency; the other child's skin was normal. A history of vitamin deficiency in these cases is rare. Regarding associated night blindness, none of those seen by me have had clinical manifestations of this condition. They were not tested by means of the photometer. I think that many of the conditions referred to as vitamin A deficiency are not that at all. Are all patients able to utilize their adequate vitamin intake?

DR. LUDWIG OULMANN: While I do not believe that this case is one of vitamin A deficiency, I think it would be easy to prove this by administering vitamin A.

DR. PAUL E. BECHET: In my opinion the keratosis pilaris in this patient bears no relation to the old lichen planus. They are two entirely different conditions.

DR. ANTHONY C. CIPOLLARO: Knowledge of the relation of vitamin A deficiency to cutaneous eruptions is of recent origin. The cases described by Frazier and Hu (Frazier, C. N., and Hu, C.-K.: Nature and Distribution According to Age of Cutaneous Manifestations of Vitamin A Deficiency: A Study of Two Hundred and Seven Cases, ARCH. DERMAT. & SYPH. **33**:825 [May] 1936) are examples of decided vitamin A deficiency and general malnutrition. I think it is a mistake to jump to the conclusion that all patients presenting keratotic lesions on the extensor surfaces have vitamin A deficiency. Before the establishment of a definite diagnosis, patients should present not only keratosis but also evidences of a deficiency of vitamin A in the blood and night blindness. The history, moreover, must reveal that the diet has been lacking in vitamin A.

DR. DAVID L. SATENSTEIN: There are many persons who do not take plenty of vitamins but who do not have any disturbances. Many persons stay out in the sun and do not get lupus erythematosus, and in some lupus erythematosus develops after a sunburn.

A Case for Diagnosis (Lichen Moniliformis?). Presented by DR. WILBERT SACHS.

Miss H. D., aged 22, was first seen by me at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Dec. 2, 1939. She stated that two years ago the eruption developed on her palms. At first there were only a few lesions present, but the number has been slowly but steadily increasing She has never had any subjective symptoms.

A case for diagnosis (lichen moniliformis?).

The patient now presents an eruption on the palms, especially on the thenar surface and somewhat on the hypothenar surface. There are numerous discrete pearly white papules from 1 to 3 mm. in diameter. They are firm and in some areas are arranged in rows. In the past two months similar lesions have developed along the folds of the fingers.

Histologic examination showed a neurodermatitic type of reaction. No definite diagnosis could be made.

DISCUSSION

DR. HOWARD FOX: I doubt whether this condition is a naevus tardus, on account of the bilateral distribution. It is also not a neurodermatitis, because of the entire lack of subjective symptoms and the absence of signs of inflammation. I do not know how to classify the eruption.

DR. DAVID BLOOM: Considering that the biopsy was performed on material from the thenar area and not from the palm itself, the hyperkeratosis seen under the microscope is pathologic and is the only conspicuous feature. The lesion should therefore be classified as some unusual form of papular keratosis.

DR. ISADORE ROSEN: While I have not seen the histologic specimen of this case, I should make a diagnosis of verruca plana. There is also one lesion on the hand which clinically suggests verruca vulgaris.

DR. LUDWIG OULMANN: In my opinion lesions which look similar to but are not verrucae planae are seen more frequently, especially on the thenar and hypothenar areas of the palms. They spread and are itchy. I believe this condition is a contact dermatitis with keratinization.

DR. MAURICE J. COSTELLO: I agree with Dr. Rosen's conception of this case. This patient has an ordinary verruca on the hypothenar eminence of the right palm, in addition to the eruption described by Dr. Sachs. I am not sure that the lesions on the thenar eminence are verrucae planae. I think that all the lesions are verrucae and that the difference in appearance is due to the difference of location on the palms, the skin of the hypothenar eminence being thicker than that of the thenar.

DR. DAVID BLOOM: The clinical and, as I understand, the histologic observations exclude the diagnosis of verruca.

DR. WILBERT SACHS: Clinically these lesions do not impress me as being hyperkeratotic. They are smooth, and although they appear vesicular they are really solid. The biopsy specimen was taken from the palm, where the horny layer is thick. While there is some increase in the thickness of the horny layer, it is not enough to indicate a keratoma of any type. I also thought of the possibility of lichen albus, but there is no microscopic evidence to corroborate such a diagnosis. There is no suggestion of verruca in the histologic slide.

Monilial Paronychia. Presented by DR. PAUL E. BECHET.

E. A., a woman aged 38, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Dec. 26, 1939, with an eruption on the tips of her fingers of four years' duration.

On examination the finger nails show discoloration, loss of luster, transverse striations and ridges and crumbling lateral edges. The tissue proximal to the nails is swollen, reddened, indurated and painful. Occasionally pus exudes from the nail beds.

Monilia albicans were cultured from the finger nails. Smears and cultures from all other parts were negative, including those from the tongue and stool.

Wassermann and Kahn reactions were negative.

DISCUSSION

DR. DAVID BLOOM: My conception of these cases has always been that the condition is due to persistent exposure to water and insufficient drying of the hands, with the formation of a favorable soil for the growth of Monilia.

DR. HOWARD FOX: The patient has ordinary paronychia, with resulting dystrophic changes in the nails. It is well known that this disease may be due to pyogenic cocci or to Monilia. I should like to know whether the presence of the causative organism is indicated by the appearance of the dystrophic changes.

DR. ANTHONY C. CIPOLLARO: Soap and water are said to accentuate this condition. In my opinion, this is based on uncertain grounds.

I think that this case is suitable for treatment with ethyl iodide inhalation.

DR. MAURICE J. COSTELLO: I see this condition frequently in women who prepare salads and in waitresses whose occupation necessitates the frequent immersion of the hands in water. I believe that soap and water make it worse.

DR. MAX SCHEER: I have seen such eruptions in men whose occupation was such as that of bartender or dishwasher, and they have been all ages and all races.

DR. GEORGE C. ANDREWS: I also believe that it is deleterious to keep the skin saturated with water.

DR. PAUL E. BECHET: I have observed a sufficient number of cases with the same symptoms and believe that monilial infection of the finger nails presents a definite clinical picture, which is not infrequently corroborated by the demonstration of Monilia albicans. The paronychia is characterized by induration, swelling and redness just proximal to the nails. Pus is uncommon, and there is little pain. The nails are striated and ridged, and their lateral edges crumble easily and are brownish. Erosion in the webs of the fingers may or may not be present. Monilial paronychia and onychia occur most frequently in stout women who do much laundry work and dishwashing. It is much rarer in men, and when it does occur it is much more common in bus boys, waiters and dishwashers.

Pigmentation of the Mouth from Bismuth. Presented by DR. MAURICE J. COSTELLO.

G. W., a housewife aged 19, born in New York, presented from Bellevue Hospital, had a chancre of the lower lip in October 1939, in which spirochetes were demonstrated by dark field examination. This was followed by a secondary lenticular papular syphilid. The Wassermann reaction of the blood at that time was 4 plus. In the latter part of November she was delivered of an apparently normal infant. Since that time she has received five injections of neoarsphenamine, five injections of bismuth subsalicylate and seven injections of bismarsen. Since her admission to the hospital she has had two injections of mapharsen. Discrete pinpoint-sized to pinhead-sized areas of black pigmentation form pea-sized patches on the tip of the tongue where it comes in contact with the bismuth line of the lower gums. Similar areas are also present on the inner surface of the lower lip. There are a few discrete pigmented lentil-sized areas of pigmentation on the hard palate.

DISCUSSION

DR. DAVID BLOOM: Pigmentation of the tongue due to bismuth must be rare, for this is the second case I have ever observed. A similar case with pinpoint-sized pigmented spots on the anterior aspect of the tongue I observed a few weeks ago at the New York City Hospital.

DR. HOWARD FOX: I saw pigmentation of the mouth but no evidence of stomatitis. While pigmentation following bismuth therapy is extremely common along the margin of the gums, it is decidedly rare on the tongue.

DR. MAX SCHEER: I agree with those who think this condition is pigmentation and not stomatitis, and for that reason I do not think it is necessary to stop the administration of bismuth. However, the dose should be reduced to one half; in that way, the pigmentation will subside and gradually disappear.

DR. MIHRAN B. PAROUNAGIAN: I never saw such decided pigmentation on the tongue as this patient presents. I have seen the condition in a number of patients on the gum line but not as pronounced as this. If I were treating the patient, I should discontinue administration of bismuth and give mercury.

DR. S. GELLIS (by invitation): I have heard it said that pigmentation indicates that a good bismuth preparation is being used, and many suggest that the administration should be continued as long as the drug produces no general harm to the patient.

A Case for Diagnosis (Pyoderma? Iododerma?). Presented by DR. MAX SCHEER.

B. A. C., a white school girl aged 17, born in the United States, was seen at Mount Sinai Hospital, service of Dr. I. Rosen, for an eruption on the legs of four and one-half months' duration.

The eruption began as small superficial papulopustules, which gradually enlarged until they attained a diameter of 2 to 3 inches (5 to 7.5 cm.). The lesions were predominantly on the posterior aspects of the calves and ankles. They varied

from ½ to 3 inches (1.3 to 7.5 cm.) in diameter and were superficial, slightly indurated, sharply defined, circinate, bluish red and plaquelike, not raised. One of the larger lesions had three pinhead-sized openings, which oozed creamy pus. The lower margin of the largest lesion was eroded. As old lesions healed, new ones appeared, so that there are small papulopustules, various-sized circinate plaques and slightly atrophic and pigmented areas.

The patient had been taking iodized salts but no medication.

The blood count showed normal results. The sedimentation rate was 18 mm. in one hour. The Wassermann reaction of the blood was negative. Graded tuberculin tests showed normal sensitivity. The report of the histologic examination was: "Skin showed necrosis and nonspecific inflammation within the corium and ulceration." The report of a later examination was: "A definite diagnosis of Bazin's disease cannot be made, but an erythema-nodosum-like lesion is conceivable. A fungous infection or a drug eruption should be ruled out. No tubercle bacilli were seen."

In spite of the cessation of ingestion of iodized salts, new lesions are constantly appearing.

DISCUSSION

DR. ANTHONY C. CIPOLLARO: The clinical features are those of iododerma. I cannot see any evidence of Bazin's disease.

DR. HOWARD FOX: It is often necessary to differentiate bromoderma or iododerma from some type of tuberculosis, such as papulonecrotic tuberculid. I think a useful point of differentiation is tenderness, which is present in bromoderma and iododerma.

DR. MAURICE J. COSTELLO: I agree that this condition is probably a drug eruption, and I suggest that the urine and blood be examined for iodides and bromides.

DR. MAX SCHEER: I mentioned Bazin's disease, first, because that was the diagnosis suggested by my associates in the clinic and, secondly, to arouse some discussion. Personally I do not think the condition is Bazin's disease, because I could follow the lesions from their incipiency up to their full development, and none developed subcutaneously and then approached the surface. They began as superficial pustules, which spread to form large plaques. My diagnosis is a drug rash, probably an iodide eruption.

Amelanotic Melanoma. Presented by DR. MAURICE J. COSTELLO.

R. S., an Austrian Jewess, a housewife aged 50, presented from Bellevue Hospital, was previously presented before the New York Academy of Medicine, Section of Dermatology and Syphilis, on Jan. 2, 1940 (ARCH. DERMAT. & SYPH., p. 175).

DISCUSSION

DR. DAVID BLOOM: When the patient was previously presented the dark, pigmented lesion in the center made me consider first of all the diagnosis of malignant melanoma with dissemination, in spite of the nonpigmented satellite lesions. I did not consider lymphangioma circumscriptum, because, among other points, the age of the patient at which the lesion appeared did not conform with that diagnosis.

DR. S. GELLIS (by invitation): When this patient was admitted to my ward at Bellevue Hospital, I entertained the diagnosis of either Kaposi's sarcoma or hemolymphangioma circumscriptum. One of the lesions was punctured, and it was found to be solid. The patient left the hospital for a short time, and when she returned new lesions were noticed on the front of her leg. Dr. Fox and Dr. Bloom suggested the diagnosis of melanoma. I should like to have suggestions as to treatment.

DR. J. FRANK FRASER: I prefer the term amelanotic melanoma.

DR. WILBERT SACHS: At the meeting of the New York Academy of Medicine, Section of Dermatology and Syphilis, I thought the condition was Kaposi's sarcoma. I should not make that diagnosis tonight, after hearing the pathologic report. Since in the microscopic description there is no mention of any changes in the lower border of the epidermis, I suggest that Perl's test be done to see if the pigment is melanin or iron.

DR. DAVID L. SATENSTEIN: Might I refer to Broder's classification of neoplasms? The patient has a better chance to live if the lesions are not excised. If radical surgical intervention is done, it must be amputation. Radium might do some good. I am not so sure that this patient will die, because I have seen patients with these lesions that are still alive after long periods. Not all cases of melanoma are fatal.

DR. MAURICE J. COSTELLO: The biopsy specimen was taken from the original lesion, which at that time was moderately pigmented. I think that the title under which this case is reported should indicate the fact that some of the lesions are melanotic and some clinically are nonpigmented. In the beginning the clinical diagnosis was difficult, because most of the lesions were nonpigmented and they suggested lymphangioma circumscriptum or Kaposi's sarcoma. The patient has had no treatment.

Charcot's Disease of the Ankle. Presented by DR. MAURICE J. COSTELLO.

G. F., an unemployed man aged 41, born in the United States, presented from the wards of Bellevue Hospital, gives no family history of syphilis. A painless swelling of the right ankle appeared four months ago. When he was admitted to the hospital, in addition to the aforementioned symptoms, examination of the joint showed crepitus and hypermobility, which were not accompanied by tenderness. Roentgenograms of the right ankle showed a fracture along the dorsal aspect of the right tarsal scaphoid, with backward displacement of the fragments. There is an extensive periarticular infiltration of the soft parts.

The patient has recently received malarial therapy for syphilis of the central nervous system. The Wassermann reaction of the spinal fluid was 4 plus, and the colloidal gold curve was tabetic in type. For the past ten months he has had lightning pains in his lower extremities and urgency of urination. In addition to malarial treatment, he has been given bismuth subsalicylate intramuscularly and sodium iodide intravenously. Therapy has had no beneficial effect on the ankle.

DISCUSSION

DR. S. GELLIS (by invitation): When this patient was first admitted to the hospital he complained of pain about his ankle, especially on pressure, over the medial aspect of the right scaphoid. He gave no history of injury to his foot. After a few days in the ward the pain disappeared, and manipulation of his ankle caused no pain, although definite crepitus was elicited. Further roentgenograms showed Charcot joint with fragmentation of the previously reported fracture. The orthopedic surgeons recommended an ankle fusion.

DR. MAURICE J. COSTELLO: I think this patient has a Charcot joint, because of the lack of pain, the preternatural mobility and the clinical and roentgenologic appearance. I do not think that the destruction has caused complete involvement of the tarsal bones.

Aberrant Hair on the Mucous Membrane of the Lower Lip. Presented by DR. MAURICE J. COSTELLO.

W. K., an electrician aged 46, born in New York, presented from Bellevue Hospital, gives no family or personal history of congenital abnormalities. About three months ago the patient felt with the tip of his tongue a hair on the mucous

membrane of the lower lip. He thought it was a tooth brush bristle, which it resembled. He pulled it out and found two hairs with their sheaths. Three weeks later he removed a hair of similar appearance from the same location. This phenomenon was repeated three times in three months. The hair in this location was ½ inch (1.3 cm.) in length, coarse and colorless. Microscopically it proved to be a terminal unpigmented hair.

DISCUSSION

DR. DAVID BLOOM: It would be of interest to study this hair under the microscope to see if it differs in any respect from the hair on the skin.

DR. LUDWIG OULMANN: Fifty years ago Max Joseph (Lehrbuch der Haut- und Geschlechtskrankheiten, ed. 2, Leipzig, Georg Thieme, 1895) mentioned the presence of hair in combination with sebaceous glands in the mucous membrane of the lip, Audry (*Monatschr. f. prakt. Dermat.* **29**:101, 1899) and Bergière mentioned the presence of hair in the mucous membrane.

Recklinghausen's Disease Associated with Eighth Nerve Deafness. Presented by DR. MAURICE J. COSTELLO.

J. B., an unemployed Irish-American man aged 38, states that there is no family history of Recklinghausen's disease. I have not examined other members of the family. The duration of the eruption is twenty-five years. It is generalized and consists of soft pedunculated herniated fibromas and irregular areas of café-au-lait pigmentation, characteristic of this disease. He also has similar lesions on the tongue and soft palate. He has had total deafness of the left ear for the past four years, which an otologist stated is due to a fibroma involving the eighth nerve. He has asymptomatic neurosyphilis. He had a chancre eighteen years ago. The Wassermann reactions of the blood and spinal fluid were positive, and the colloidal gold curve was 0001221000. Antisyphilitic treatment at present consists of injections of mapharsen.

DISCUSSION

DR. DAVID BLOOM: While the commonest lesions of Recklinghausen's disease are pigmentation, tumors of the skin, peripheral nerves and cranial nerves are occasionally encountered and are often discovered at autopsy. Bilateral tumors of the acoustic nerve causing sometimes complete deafness have been reported. In order to state definitely that no other member of the family is affected, one has to examine personally all the members, for pigmentation and a few cutaneous tumors are usually overlooked or ignored.

DR. ISADORE ROSEN: This case is interesting because all types of complications are frequently seen associated with Recklinghausen's disease. I recall an instance in which the late Dr. Goldenberg was called in to see a patient in the urologic service of Mount Sinai Hospital for some renal condition. The patient had the clinical symptoms of mild Recklinghausen's disease; in the discussion of the case Dr. Goldenberg emphasized the importance of looking for malformations of the kidney, as they occasionally occur in connection with that disease. It was found that the patient had a horseshoe kidney, and it was fortunate that the condition was recognized before surgical intervention was done.

DR. J. FRANK FRASER: I agree with the otologist whose theory is that the deafness in this case is due to neurofibroma involving the eighth nerve. The peripheral nerves of the skin are not the only ones involved in the course of Recklinghausen's disease, and physicians are all aware of the deformities due to involvement of the spinal nerves. Involvement of the cranial nerves also occurs and much more frequently than is generally supposed.

In regard to prognosis, one must keep in mind the fact that sarcoma develops in about 13 per cent of all cases of Recklinghausen's disease. The percentage in Geschichten's series was 20 per cent. I have observed 2 cases of subepidermal sarcoma in Recklinghausen's disease during the past year.

DR. MAURICE J. COSTELLO: I have seen several patients who had foot drop resulting from osseous rarefaction of the vertebral column in the lumbosacral region.

Scleroderma, Sclerodactylia. Presented by DR. E. WILLIAM ABRAMOWITZ.

O. H., a married man aged 25, was first presented before the New York Academy of Medicine, Section of Dermatology and Syphilis, on March 4, 1924 (ARCH. DERMAT. & SYPH. **10**:368 [Sept.] 1924). Subsequently I presented him at another meeting in 1926 (ibid. **15**:353 [March] 1927). The last presentation was by Dr. Bloom in 1930 (ibid. **22**:928 [Nov.] 1930).

At present all the fingers and toes are shriveled. The skin in these areas is hidebound and livid. The extensor area of the right elbow also shows a scleroderma, with apparent calcification. The rims of the ears and the tip of the nose are partially destroyed and atrophic. The patient has always had a tendency to have cutaneous infections. Recently cutaneous abscesses have developed on the spine and over other bony prominences, and because of his poor nutrition these abscesses break down and form ulcers which are slow in healing. He is at present receiving vitamins A and D in addition to a high caloric diet and local applications of gentian violet.

The diagnosis is scleroderma confined to the terminal parts of the body, the underlying cause of which has not yet been determined, owing to the poor cooperation of the patient. Various laboratory tests are now being performed.

DISCUSSION

DR. DAVID BLOOM: This man was also presented in 1926 (ARCH. DERMAT. & SYPH. **15**:353 [March] 1927) before the Brooklyn Dermatological Society. He was first presented (ibid. **10**:368 [Sept.] 1924) as having acrodermatitis pustulosa hiemalis, because of ulcers and exacerbations during cold weather. A diagnosis of epidermolysis bullosa was also considered, because the ulcers resembled broken bullae. These diagnoses are not infrequently made in cases of sclerodactylia which are not recognized as such. In 1930 I presented this patient (ibid. **22**:928 [Nov.] 1930) with the diagnosis of progressive symmetric scleroderma. One finds this term, particularly in the French literature, in contrast to generalized scleroderma, to designate those conditions which start with involvement of the fingers and toes, and may be confined to these and other distal areas of the body or may extend to the hands, wrists, forearms and other areas. "Generalized scleroderma" spares, at least at first, the fingers and toes. This patient shows, besides the acrosclerosis, also atrophy of the skin over the bony prominences of the elbows, vertebrae and shoulders, associated in some places with ulcerations.

DR. HOWARD FOX: In my opinion, this case is by no means a typical one of scleroderma but a most unusual one. In the ordinary case of scleroderma of the progressive type, the skin of the face is usually hidebound. In this case it can be easily pinched up between the fingers.

DR. DAVID BLOOM: The reason for the gangrene in this case, which led to loss of part of the fingers, nose and ears, is the hidebound condition of the skin, leading to atrophy and destruction of the underlying soft tissues and bone. In Raynaud's' syndrome the cause of gangrene is the frequent constriction of the blood vessels. Although the syndrome of Raynaud's disease may be present in cases of scleroderma, for both conditions are due to disturbance of the vegetative nervous system, this case cannot be designated one of "Raynaud's disease."

DR. MAX SCHEER: There are two types of scleroderma, the type that involves the trunk and later on may affect the face, and the type to which this case belongs, true acrosclerosis, which begins on the extremities and ends on the face and never involves the trunk or other parts of the body.

DR. GEORGE C. ANDREWS: There is a disease described as acrosclerosis, and I think this case fits into that category.

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

E. W. Abramowitz, M.D., *Chairman*

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Jan. 2, 1940

Kaposi's Sarcoma. Presented by Dr. Louis Tulipan.

M. C., a Negro aged 56, presented from Bellevue Hospital, about nine months ago first noticed swelling and an eruption on the right hand. It then appeared on the left hand and shortly thereafter on the feet. The hands and feet were edematous, with multiple bluish nodules, pigmented patches and ulcerations, especially over the toes and fingers. He had been treated for syphilis at one of the city clinics during the year.

The Wassermann reaction of the blood on admission to Bellevue Hospital was 4 plus. Physical examination revealed nothing unusual except that the blood pressure was 102 systolic and 50 diastolic. The icteric index was 18, and the differential white blood cell count was normal. The patient complained of precordial pain. Roentgenograms of the hands showed generalized bony atrophy and flexion deformities of the fingers. Histologic examination of sections of the skin showed numerous dilated capillaries, with decided proliferation of connective tissue and many round and spindle cells, in places appearing sarcomatous. There were foci of hemorrhages in the surrounding tissue and hypertrophy of the horny layer.

About three months after admission to the hospital, after an attack of precordial pain, he became stuporous and died. The cause of death was coronary thrombosis.

DISCUSSION

Dr. Charles Wolf: I take for granted that the histologic examination has proved the diagnosis. The interesting feature is the short duration of an extensive eruption of Kaposi's sarcoma. Kaposi's sarcoma is generally considered a slow, insidiously progressive disease.

Dr. Eugene T. Bernstein: I think that the coexisting syphilis can be regarded as a contributory factor in the spreading of the eruption, and the spreading to such an extent may be due to lessening of the resistance of the patient. I doubt, therefore, that ten months' duration disproves the diagnosis of Kaposi's sarcoma.

Dr. Isadore Rosen: I wonder whether this patient has taken any iodides. It is well known that iodides may produce cutaneous lesions of all types. The lesions of Kaposi's sarcoma are usually slow in development, while those in this patient developed rapidly. I therefore suggest the possibility of a connection between this eruption and the treatment he has had for his syphilitic infection, which included arsenicals.

Dr. Louis Tulipan: The patient has had no iodides but has received the regular antisyphilitic treatment with a bismuth compound and arsenic.

Dr. Maurice J. Costello: The only therapy this man has received has been bismuth subsalicylate. He has had solution of potassium arsenite U. S. P. only since his admission to Bellevue Hospital, which was three weeks ago. There has been no appreciable change in the eruption since that time.

Dr. Louis Tulipan: The interesting feature about this case is that Kaposi's sarcoma is extremely rare in Negroes. I think there are only about 4 or 5 cases reported in the literature. Again, there is the fact that the condition started on the hands instead of on the feet. In regard to the rapid developmen of the eruption and the destructive lesions, I believe that poor peripheral circulation may tend to rapid destruction and breaking down of lesions. One often sees lymphedema

and verrucous lesions in cases of Kaposi's sarcoma. Where there is poor peripheral circulation, as here, plus lymph stasis and edema, there might, therefore, be rapid destruction. I think that is the only plausible explanation.

A Case for Diagnosis (Kaposi's Sarcoma?). Presented by DR. FRANK C. COMBES.

R. S., a woman aged 50, is presented from Bellevue Hospital, complaining of an eruption involving the right leg, of five months' duration. Examination shows over the lower part of the right leg a patch of closely aggregated papules varying in size from that of a pinhead to that of a pea and in color from pink to dark purple. There are also discrete lesions on the front of the leg which have appeared during the past week.

The Wassermann reaction was negative.

NOTE.—Subsequent to this presentation, histologic examination showed a malignant amelanotic melanoma.

DISCUSSION

DR. CHARLES WOLF: I should like to suggest the diagnosis of hemangiolymphangioma circumscriptum. The lesions appear hemorrhagic. They are soft, circumscribed and superficial. In the early manifestations of Kaposi's sarcoma the lesions are apt to be infiltrated. One does not see discrete vascular lesions, although there may be vascular lesions in accompaniment with the infiltrations. However, to find a discrete vascular lesion in a case of Kaposi's sarcoma is rare.

DR. LEO SPIEGEL: I saw this woman about three or four weeks ago and my impression agrees with that of Dr. Wolf, that the condition is hemangiolymphangioma circumscriptum.

DR. DAVID BLOOM: This woman impresses me as having a malignant melanoma, with less pigmented satellite lesions around a deeply pigmented primary lesion. The location and particularly the rapid development in a patient of such advanced age speak against the diagnosis of lymphangioma circumscriptum.

DR. FRANK C. COMBES: I understand how the diagnosis of hemangiolymphangioma circumscriptum is entertained. That condition was the one I considered the first time I saw this patient, and I did not think of Kaposi's sarcoma as a diagnosis. The little nodules were pearly and looked like deep vesicles, but on being opened they were found to be solid. The age of the patient is somewhat against lymphangioma; it is usually seen in much younger persons. It is possible for lymphangioma to occur in this location, but it is more common on the upper parts of the extremities. I have never seen Kaposi's sarcoma, if the condition in this case proves to be that, at such an early stage, and I do not know just what it looks like at that time. One may see the angiomatous stage, in which there is little infiltration and little proliferation other than that which occurs in the blood vessels. The picture has changed some since this patient was first seen, and tonight the lesions are dusky red or blue, and there is scaling on some of them and some confluence. New lesions have appeared in the past few weeks, especially on the anterior part of the leg. In reference to melanoma, these lesions at their inception contain no pigment. They are clear and pearly. The pigmentation is secondary. In addition, there was no preexisting lesion of any type. The condition may be an amelanotic melanoma, but I do not recall having seen a patient with this condition.

Epidermolysis Bullosa Acquisita. Presented by DR. LOUIS TULIPAN.

S. B., a woman aged 57, presented from Bellevue Hospital, was previously presented at a meeting of the Bronx Dermatological Society (ARCH. DERMAT. & SYPH. **40**:1016 [Dec.] 1939).

At present the patient exhibits few lesions, and in fact, this is the best she has been in the past year. There are remains of healed bullae on the dorsa of

the hands, the elbows, the buttocks and the right border of the tongue. On the extensor surfaces of the forearm are numerous grouped milia-like cysts. There are a few vesicles on the heels.

The patient was given large doses of viosterol in oil for three months, without effect. At present she is receiving 5 cc. of concentrated liver extract weekly; she has been receiving this for the past fifteen weeks.

Epidermolysis Bullosa. Presented by Dr. Timothy J. Riordan.

A. M. S., a girl aged 2½ years, is presented from the New York Foundling Hospital. The eruption was first noticed when the child was 3 days old. It was located on the hands and feet, including the fingers and toes, and consisted of tense bullae arising from normal skin and erythematous areas covered by crusts resembling impetigo. Similar crusted lesions were scattered over the trunk and buttocks. There were many depigmented atrophic scars of previous lesions. No milia were observed.

DISCUSSION OF CASES OF DR. TULIPAN AND DR. RIORDAN

Dr. David Bloom: The woman presented by Dr. Tulipan has all the features characterizing epidermolysis bullosa dystrophica, namely, epidermal cysts, atrophy of the skin, involvement of the mucous membranes, with resulting scars, and dystrophy and shedding of the nails. The child presents the same condition, with greater intensity. In the first patient the term acquisita is not justified, and the term tarda should be substituted, for unless it can be proved definitely that the condition is due to some external agent, it should be considered hereditary. The fact that in most cases of epidermolysis bullosa dystrophica there is a recessive mode of inheritance explains the absence of the disease in other members of the family.

Dr. Eugene T. Bernstein: I am afraid to entertain another diagnosis in the first case, but the condition in the second case impresses me as pemphigus vulgaris. With all respect to the diagnosis made at the Bronx Dermatological Society and with all respect to the histologic examination, I say that in epidermolysis bullosa one often sees involvement of the tongue, and the cystic lesion on the elbow favors the diagnosis of epidermolysis bullosa. The scratch marks are significant. They were produced about ten days ago and at present impress me as a symptom of Köbner's disease. On the other hand, they may be a masquerade for a Nikolsky sign (detachment of the upper layer of the epidermis).

Dr. Frank C. Combes: It was my impression that in a case of the hereditary type of epidermolysis bullosa a biopsy specimen taken from uninvolved skin would show alterations in the elastic tissue, whereas with the acquired type these alterations occur only in the areas in which the bullae occur. Is that true?

Dr. David Bloom: In the few cases of my personal experience I have not succeeded in finding elastic tissue absence or deficiency in the normal-appearing skin of these patients. The reports in the literature vary a great deal in regard to this pathologic feature. This is the reason why elastic tissue deficiency cannot be considered as the cause or, at least, as the only cause of epidermolysis bullosa.

Dr. Louis Tulipan: In answer to Dr. Bernstein, my case was at first considered one of possible pemphigus vulgaris because of the bullae, but I think that can be ruled out on account of the epidermal cysts. Then again, I agree with Dr. Bloom that the condition in this case is really a hereditary dystrophic type, in spite of the fact that it has been called the acquired type. This patient shows epidermal cysts, which is the usual condition in congenital cases. I presented a case here (Arch. Dermat. & Syph. **37**:22-26 [Jan.] 1938) of the dystrophic type in a baby whose entire body was practically covered with lesions and scars and who had lost all the nails. I feel that this patient's condition resembles that one closely except that it is not so generalized. As to the absence or diminution of elastic tissue in the unaffected skin, that varies in different cases.

Parapsoriasis. Presented by DR. MAURICE J. COSTELLO.

H. L., a man aged 32, is presented from Bellevue Hospital, complaining of an eruption on the arms, thighs and abdomen of nine months' duration. There is slight itching. The patient applied 10 per cent crude coal tar, without any effect, and then 5 per cent chrysarobin was used until it caused a dermatitis, but the character of the lesions did not change.

Examination shows in the aforementioned areas several well defined, erythematous patches, varying in size from 2 to 5 cm. in diameter. There is a fine superficial scaling on the lesions.

Examination of scrapings showed no fungi. Histologic examination showed parapsoriasis.

DISCUSSION

DR. HARRY KEIL (by invitation): The case appears to be one of parapsoriasis en plaques, but it should be followed. The ordinary criteria required for this diagnosis are fulfilled, though perhaps there is more pruritus than one would expect. However, I believe that the eventual prognosis in this case is bad.

DR. CHARLES WOLF: If my memory serves me correctly, articles by Dr. Keil give the impression that the diagnosis of mycosis fungoides could be made in the early stages.

DR. HARRY KEIL (by invitation): I can point to a case that was presented last month at the monthly staff conference of the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, in which the patient showed a typical parapsoriasis en plaques of twelve years' duration, without any infiltration to speak of. Yet a histologic examination showed changes considered typical of mycosis fungoides. The clinical appearance of the eruption, even after twelve years, was that of typical parapsoriasis en plaques. In Dr. Costello's case, however, one is dealing with a person who has had an eruption of only nine months' duration. I do not believe it is possible to rule out mycosis fungoides simply because the histologic examination does not show the changes considered pathognomonic of this disease. I pointed that out very clearly in the articles mentioned by Dr. Wolf (ARCH. DERMAT. & SYPH. (*a*) **37**:465 [March] 1938; (*b*) **38**:545 [Oct.] 1938). In my original case three specimens of skin were taken for biopsy, none of which showed the alterations of mycosis fungoides, but four years later (about eight years after onset) another biopsy of skin revealed the typical changes of that disease. I do not want to go into the question of whether mycosis fungoides is such from the beginning, as this question often resolves itself into a matter of quibbling, but the fact remains that there are now available a tremendous number of instances of typical clinical parapsoriasis en plaques that has developed eventually into mycosis fungoides.

DR. WILBERT SACHS (by invitation): At the conference mentioned by Dr. Keil I made the statement that although the patient's clinical appearance was that of parapsoriasis, the condition was mycosis fungoides from the beginning. Cases with the clinical picture of parapsoriasis microscopically may be either parapsoriasis, and remain so, or mycosis fungoides from the start.

DR. MAX SCHEER: I think that Dr. Keil's case does not bear out Dr. Sachs's statement, because his patient for a number of years had no evidence of mycosis fungoides histologically, and it developed only some eight years after the onset of the disease. The whole question, of course, is rather complicated. There is no doubt that cases of parapsoriasis are clinically observed that remain as they are, but there are others which may show mycosis fungoides from the start or which may show it only many years later. I do not think it is correct to assume that in all cases of parapsoriasis the condition is mycosis fungoides, but in a certain number of them this disease develops. That was recognized by Brocq in his textbook (Brocq, L.: Cliniques dermatologiques, Paris: Masson et Cie, 1927, p. 451), in which he reported cases of parapsoriasis which terminated in mycosis fungoides.

DR. ISADORE ROSEN: I agree with those who say that parapsoriasis may begin as such and terminate as such after many years. There are instances, however, in which mycosis fungoides begins with lesions that resemble parapsoriasis both clinically and histologically and that later show all the clinical features and pathologic changes of mycosis fungoides. It is well known that patients sometimes have psoriasis for many years, the diagnosis having been confirmed by microscopic examination, and then suddenly present both clinical and histologic features of mycosis fungoides. It is difficult to explain this change.

DR. PAUL GROSS: In several cases I have observed a minor feature which would seem to be characteristic of parapsoriasis en plaques, namely, the evolution of the eruption. The early lesions begin on the distal parts of the extremities, and as the eruption develops, new lesions appear on the thighs and arms and finally on the trunk. Not infrequently this can even be ascertained in taking the patient's history. It would be interesting to hear the experience of the members on that point. Dr. Rosen has brought up the fundamental question of mycosis fungoides in relation to parapsoriasis en plaques, as well as psoriasis. One theory is that mycosis fungoides is a lymphoblastoma from the beginning, while more recently the idea has been expressed that benign dermatoses may produce a disturbance of the reticuloendothelial system which is responsible for the lymphoblastic development. When this question is settled, one will be able to make the diagnosis of parapsoriasis en plaques with less hesitation than now, especially after the valuable contribution of Dr. Keil.

DR. E. WILLIAM ABRAMOWITZ: I am glad that Dr. Gross specified the en plaques variety of parapsoriasis. I do not think the other types of parapsoriasis ever develop into mycosis fungoides.

DR. HARRY KEIL (by invitation): With regard to this problem, there are two sets of observations that have to be taken into consideration. First, how did this concept originally arise? The concept was first established on the basis of 3 cases, 2 reported by Unna, Santi and Pollitzer (*Monatsh. f. prakt. Dermat.* **10**:404, 1890) and 1 by Brocq (*Rev. gén. de clin. et de thérap.* **11**:577, 1897). Of the first 2, Santi's case turned out to be one of mycosis fungoides; as for the second case, I can only say that Dr. Pollitzer told me personally that there was no histologic evidence of mycosis fungoides, but he knew nothing of the eventual clinical course (personal communication, Feb. 10, 1937). In regard to Brocq's case, it is little known that this patient had complained of generalized pruritus some two years before the eruption appeared. Moreover, Brocq diagnosed the condition in many subsequent cases as parapsoriasis, but nearly all were later considered instances of mycosis fungoides; proof of this may be found in Civatte's thesis (Les parapsoriasis de Brocq, Thesis, Paris, no. 216, 1906, Paris, G. Steinheil, 1906).

The second consideration is that there are now collected numerous cases of parapsoriasis en plaques that have been observed for twenty years or more. For example, in Savatard's patient mycosis fungoides developed after forty-one years (*Brit. J. Dermat.* **50**:150, 1938). The case reported by Gougerot and Burnier is a classic example (*Bull. Soc. franç. de dermat. et syph.* **41**:1528, 1934). I think there will be an increasing frequency of such findings now that these cases are being followed and studied more thoroughly.

Finally, may I add to the records two observations of unusual interest? The first is a quotation from a letter written to me by Dr. Udo J. Wile (March 30, 1938):

". . . I am quite sure that I could find from 8 to 12 of my own in which I have been able to see the metamorphosis of parapsoriasis en plaques into mycosis fungoides, and I entirely share your view that whenever I encounter a case of disseminated parapsoriasis it always bespeaks for me a potential lymphoblastomatous development."

In a recent discussion (ARCH. DERMAT. & SYPH. **37**:117 [Jan.] 1938) Dr. G. M. MacKee mentioned the case of a girl afflicted with parapsoriasis that

developed subsequently into mycosis fungoides. In response to my inquiry, Dr. MacKee (personal communication, April 9, 1938) stated that the patient was now a grown woman and that the dermatologists who were watching her in Lima, Peru, have also made a diagnosis of mycosis fungoides. This observation is of great interest, for it concerns a case in which the condition had its onset early in the patient's life.

DR. MAURICE J. COSTELLO: The lesions in this case began on the extremities, as Dr. Gross mentioned, and spread to the center of the body. It seems to me a rather interesting point that in cases of mycosis fungoides itching is an important feature and is fairly constant, while it is practically never associated with parapsoriasis. Mycosis fungoides responds readily to subfractional (38 r) doses of roentgen rays, and parapsoriasis is resistant and persistent in spite of roentgenotherapy. The lesions of mycosis fungoides are polymorphous and changeable, and those of parapsoriasis are polymorphous and stationary. In view of these facts it is curious that these two eruptions should in any way be related.

Recurrent Symmetric Herpes Simplex of the Fingers. Presented by DR. FRANK C. COMBES and DR. MAURICE J. COSTELLO.

T. S., a man aged 30, presented from Bellevue Hospital, was previously presented at a meeting of the Manhattan Dermatologic Society (ARCH. DERMAT. & SYPH. **39**:366 [May] 1938).

The case is presented because of its unusual features of regular seasonal occurrence (in May and October) over a period of fifteen years, in addition to its symmetric location on the fingers of both hands.

DISCUSSION

DR. EUGENE T. BERNSTEIN: I consider this case as one of fixed drug eruption. Has the patient ingested any drugs, such as phenolphthalein?

DR. E. WILLIAM ABRAMOWITZ: I am inclined to agree with Dr. Bernstein that this condition is a fixed drug eruption of the herpetic type. The patient on occasion takes a proprietary preparation which is reported to contain acetylsalicylic acid, acetanilid and potassium bromide.

DR. MAURICE J. COSTELLO: The patient states that he has had this eruption for fifteen or sixteen years, and it has recurred in the same locations about four times a year. We have questioned him about drugs, and there is certainly no history of ingestion of any. I gave him six or eight vaccinations with cowpox, and the interval between the last attack and the one he has today is the longest he has ever had in sixteen years, namely, about nine months.

DR. HERMAN GOODMAN: How many times did the cowpox "take"?

DR. MAURICE J. COSTELLO: There were one "take" and about seven immune reactions, which were represented by a papular reaction which lasted from two to five days.

DR. MARION B. SULZBERGER: Herpetic eruptions confined to the fingers are perhaps not as rare as is generally supposed. They were well described by Dr. William Frei (*Dermat. Wchnschr.* **93**:1508 [Sept. 26] 1931). The herpes simplex nature of an eruption is usually easy to prove by means of inoculation of a rabbit's cornea. I think that should be done in this case. I should like to point out the fact that because one can recover herpes virus from the lesion does not rule out a fixed eruption. In some cases recurrent fixed localized herpes simplex can occur after ingestion of a certain food or drug, and in such cases one can recover herpes virus; and in these cases there might be a synergistic relation between the virus and the ingested drug or food in producing what is in a certain sense a "fixed" herpetic eruption.

DR. LOUIS TULIPAN: I think it would be interesting to bring up the question of the effect of vaccination on herpes, as long as it has been mentioned in connec-

tion with this case. I believe that physicians who have done any work on this subject should report their results, as some people believe that vaccination is almost the specific treatment for this type of eruption. I have followed this for three years in about 15 cases, and I find that vaccination does little good. It does seem sometimes to increase the intervals between the attacks. Whether it is the effect of the vaccination or not I do not know, but I am sure of one thing: whether one, two or three vaccinations are given and whether the vaccination "takes" or not makes little difference, as the patients get recurrences sooner or later.

DR. HERMAN GOODMAN: In a long period of observation, the diagnosis of herpes simplex having been made, the patient has been found to give a positive "take" with vaccine obtained from the department of health. This result was not influenced by the history of past vaccination. Repetition of the vaccination within a few days or weeks after a positive "take" has not resulted in secondary positive reaction. There is only one such "take." Until a few months ago when I discussed this question with Dr. Chargin, it was my impression that the patients treated by vaccination had been cured. It is possible that these patients went elsewhere for treatment on recurrent attacks following the vaccination.

DR. MAURICE J. COSTELLO: We have treated many patients with herpes simplex in private practice and in the clinic. I think in a certain percentage of the cases the vaccination is of no value. In another, smaller percentage, about 40 per cent, it increases the intervals between attacks and decreases the severity and duration of the attacks.

DR. HERMAN GOODMAN: When I discussed herpes simplex, the diagnosis excluded that due to the ingestion of drugs, such as phenolphthalein.

DR. MARION B. SULZBERGER: Dr. Wise and I first called attention to our results with this method of treatment in the Year Book of Dermatology and Syphilology for 1934 (Chicago, The Year Book Publishers, Inc., 1934, p. 426). We have discussed smallpox vaccination for recurrent herpes simplex in subsequent Year Books (ibid., 1936, p. 156; 1937, p. 430; 1938, p. 452). I think our statements correspond with those of Dr. Costello. The evidence of the beneficial effects of repeated vaccination seems to be undeniable in certain cases of recurrent herpes, at least as far as lengthening the interval between attacks is concerned. I recall particularly the case of one of my secretaries who had recurrent herpes simplex regularly at about monthly intervals. After a series of smallpox vaccinations she had an interval of freedom lasting over two years. After this two year interval the herpes simplex recurrences recommenced; she had attacks at intervals of two or three months, the interval getting shorter each time. I vaccinated her again on three successive occasions, and again there was a remission of a year. I have had a number of similarly successful cases. However, in others I have seen no benefit from vaccination. The question of repetition of vaccination after one has had one "take" is an interesting one. I do not agree with Dr. Goodman. It is true that the "take" with accelerated response signifies a state of allergy to the cowpox virus, but in treating herpes simplex it is not necessarily the state of allergy to pox virus which is significant. Therefore, one cannot assume that the state of allergy to the herpes virus necessarily parallels the sensitivity to pox virus; and one cannot predict from the local result of vaccination—from either the "take" or the "nontake"—what will be the cross immunologic effect on the patient's susceptibility to herpes virus.

DR. DAVID BLOOM: I have treated with this method only a small number of patients with recurrent herpes, but I have obtained in some of them spectacular results. One of these patients was a girl, a medical student, who was inconvenienced for many years by the monthly recurrence of grouped vesicles over the lumbar and sacral region. Very few vaccinations freed the patient from this eruption for at least one year. Even if this method of treatment is not successful in all cases of recurrent herpes, it is today the method of choice and should be tried in every case.

DR. PAUL GROSS: The discussion on the treatment of recurrent herpes simplex with smallpox vaccine certainly is interesting, but even the originator of this treatment has not claimed more than 50 per cent of success. As Dr. Sulzberger pointed out, there is in use now a substitute and not a specific vaccine. Since there is no other therapy for recurrent herpes simplex, the use of the cowpox vaccine, a simple and fairly innocuous treatment, should not be discouraged.

DR. MARION B. SULZBERGER: I do not think the procedure is entirely harmless and would like to cite an example (not for the record).

DR. E. WILLIAM ABRAMOWITZ: Will Dr. Combes and Dr. Costello report on this case again, particularly on the results of the administration of a test dose of the proprietary preparation that the patient has been taking? Perhaps the patient will not need the vaccination at all.

Lupus Erythematosus with Involvement of the Palpebral Conjunctiva.

Presented by DR. FRANK C. COMBES and DR. MAURICE J. COSTELLO.

F. C., a woman aged 37, presented from Bellevue Hospital, was previously presented at a meeting of the Bronx Dermatological Society (ARCH. DERMAT. & SYPH. **38**:671 [April] 1938).

At the present time the eruption, which is erythematosquamous and atrophic, involves the lower eyelids, the chest and the scalp, where there is a palm-sized area of permanent alopecia on the vertex. There is a moderate eversion of the lower eyelids.

The patient was given an intradermal test with old tuberculin in a dilution of 1 to 10,000. A bullous reaction occurred, surrounded by a hand-sized area of erythema and edema, during the existence of which improvement in the eruption was evident. There was also a similar but less severe reaction with a dilution of 1 to 10,000,000. Both reactions can still be seen on the flexor aspect of the left forearm.

DISCUSSION

DR. CHARLES WOLF: The only point I wish to discuss is the relation between the appearance of the conjunctiva and the disease. If the presenters believe that there is involvement of the conjunctivas, I fail to see it. During involvement of the buccal mucous membrane in cases of lupus erythematosus, superficial ulcerations are seen. Here there is only a mild congestion which is due to the ectropion because of the cicatricial effect on the lower eyelid. Therefore, the inclusion of involvement of the conjunctival mucous membrane is not justified from the appearance. Another point about lupus erythematosus is the response to sulfanilamide therapy in refractory cases. I have used it in 3 patients who have had the disease for many years, and who have cleared up with bismuth therapy and other measures and then had a relapse later. My method of using the drug is the fractional method, giving small doses, of 5 grains (0.32 Gm.), three times daily for a week and following this with a rest, checking up, of course, on the blood before and during the treatment.

DR. DAVID BLOOM: What Dr. Wolf just said concerns me, for I presented this patient at this section meeting (ARCH. DERMAT. & SYPH. **38**:67 [Oct.] 1938) just for the purpose of demonstrating lupus erythematosus of the conjunctiva of the lower eyelid. Ulceration is not a necessary feature of lupus erythematosus of the mucous membranes. In this patient not only is the edge of the eyelid affected, suggesting ectropion, but also the inner aspect of the lid, independently of the edge.

DR. PAUL GROSS: This patient is presented particularly on account of the positive reaction to tuberculin. More recently, Marchionini (*Arch. f. Dermat. u. Syph.* **158**:505, 1929) reported on the results with a Bessau modification of the tuberculin test, and found positive reactions in about 60 per cent of the cases of lupus erythematosus. This percentage has been found rather consistently by other investigators too. Using tuberculomucin many years ago for treatment of different

types of tuberculosis, I also obtained a few excellent results in cases of lupus erythematosus. Even with the advent of sulfanilamide, one ought not to forget the well known fact that lupus erythematosus is a cutaneous manifestation resulting from an infectious focus which may be tuberculous or nontuberculous.

DR. E. WILLIAM ABRAMOWITZ: When there is a positive tuberculin reaction reported in a case of lupus erythematosus there should be an accompanying biopsy to exclude lupus vulgaris of a superficial type. I agree with Dr. Wolf in the use of small doses of sulfanilamide in cases of lupus erythematosus, with the accompanying safeguard of blood counts. I use small doses for several weeks and alternate with quinine if the patient can tolerate it. I think this patient presents lupus erythematosus of the palpebral conjunctiva.

DR. FRANK C. COMBES: I agree with those who consider the probability that the tubercle bacillus is either actively present in the lesion in this case or its toxins are responsible for the development of the lesions. This hypothesis is interesting, since the patient improved as a result of the tuberculin test. The reactions were pronounced, with large bullae and considerable infiltration, even with 1 to 10,000 dilution, and a definite reaction was present even with a dilution of 1 to 1,000,000.

DR. MAURICE J. COSTELLO: The patient was presented because of the hypersensitivity to tuberculin. Dr. Canizares and I have observed about 10 patients with lupus erythematosus of the discoid type at Bellevue Hospital, who were treated with small doses of sulfanilamide three times a day for many weeks. We think this patient is the only one who showed any improvement.

Unilateral Acneform Eruption Following Bell's Palsy. Presented by DR. FRANK C. COMBES.

Y. L., a woman aged 19, presented from Bellevue Hospital, was previously presented at a meeting of the New York Dermatological Society on Oct. 24, 1939 (ARCH. DERMAT. & SYPH. **41**:795 [April] 1940).

The condition has been improving.

DISCUSSION

DR. EUGENE T. BERNSTEIN: This patient does not have unilateral involvement. She has also an acneform eruption on the opposite side, but it is more pronounced on the left side where she had the Bell's palsy. Perhaps it is a case of locus minoris resistantiae, meaning the condition is a trophodermatosis, a lessening of the trophic response. She probably has a more pronounced involvement on the one side due to the lesion of the nerve.

DR. HERMAN GOODMAN: Many cases of petrolatum dermatitis were reported from Germany during the World War, from 1914 to 1918. The preparation the patient said she applied was possibly not the cold cream of the United States Pharmacopeia made with almond oil and sodium borate. The term "cold cream" is applied to any form of grease which has the appearance of being white. This girl may have had dermatitis venenata from the active ingredient in the grease which she applied, with the addition of massage and heat resulting in her present condition.

DR. H. VICTOR MENDELSOHN (by invitation): I saw this patient for the first time about four months ago. At that time she presented active acne over the entire left cheek and a few insignificant papules on the right cheek. The predominance of lesions on the left side of the face was so overwhelming that one was justified in considering the eruption unilateral. In my opinion the condition is not dermatitis venenata but acne, the result of a peculiar localized sensitivity caused by the use of a "vibrator" and/or the application of cold cream. This type of cutaneous sensitization is unusual, but it may occur. I recently read a report (Kahn, I. S.: *J. Allergy* **10**:235 [March] 1939) of a case in which unilateral facial acne occurred after a positive diagnostic intranasal application

of pollen on the same side and reappeared at the sensitized site on four separate occasions in the course of specific treatment when an overdose was given. The patient had had no acne previously, during or subsequent to the period of observation.

DR. PAUL GROSS: Regarding Dr. Goodman's remarks, my own experience with European "vaselinoderma" was that it was due to the fact that the American petrolatum was not available during the years of the World War and the postwar period.

DR. FRANK C. COMBES: Kromayer once stated that the German petrolatum was not fit for any skin. This patient had no dermatitis at any time. I agree with what Dr. Bernstein said. She had a mild acne which was aggravated by the Bell's palsy, the massage and the cold cream. Which one of these agents, if any, was responsible it is impossible to say. I imagine it was the cold cream. The left side of her face is now covered with pitted scars, while the right is free. When I first saw her the left side was literally peppered with comedos and pustules.

Scleroderma (Progressive Type). Presented by DR. HENRY D. NILES.

R. D., a man aged 26, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, complaining of an eruption involving the arms and legs, the face, neck and trunk of one year's duration. The condition started with tight thick skin on the right hand, later on the legs and then on the trunk, face and neck. It is rapidly spreading and becoming worse. On the legs and on the arms, especially on the calves and forearms, the skin is hardened and tight, without inflammatory changes, but shiny and apparently adherent to the subcutaneous tissue. On the periphery of these regions there are erythematous infiltrations, and the progressive stages are visible as smaller, lentil-sized and coalescent white spots. These white spots and slight erythematous changes are present also on the upper part of the chest and back, on the outer sides of the arms and on the neck; also, extending to the adjacent scalp are erythematous changes. In some places there is atrophy beginning with cigaret-paper-like skin. There is generalized lymphadenopathy. General physical examination reveals nothing abnormal except the skin. The blood pressure is 112 systolic and 74 diastolic.

Roentgenograms of the chest were normal. Roentgenograms of the teeth showed slight periapical changes, with alveolar recession and pericemental widening. The Wassermann and Kahn tests of the blood on Nov. 10, 1939, showed the serum deeply hemolyzed, and on November 14 there was an anticomplementary reaction, 1 plus. The basal metabolic rate was + 20 per cent. Examination of the urine for creatine gave negative results. Examination of the blood showed 10 mg. calcium, 13 mg. urea, 2.4 mg. uric acid and 60 mg. sugar per hundred cubic centimeters. A blood count on November 11 showed 7,550,000 erythrocytes per cubic millimeter, 114 per cent hemoglobin and 9,400 leukocytes per cubic millimeter, with a differential count of 59 per cent polymorphonuclear leukocytes, 36 per cent lymphocytes, 2 per cent eosinophils and 3 per cent monocytes. On November 15 examination showed 7,350,000 erythrocytes per cubic millimeter, 121 per cent hemoglobin and 7,400 leukocytes per cubic millimeter, with a differential count of 48 per cent polymorphonuclear leukocytes, 32 per cent lymphocytes, 15 per cent eosinophils, 1 per cent basophils and 4 per cent monocytes. On December 15 there were 7,430,000 erythrocytes per cubic millimeter and 138 per cent hemoglobin. There was 70 per cent elevation of the cell volume. The blood volume was 130 cc. per kilogram of body weight (the normal being 72 to 100 cc. per kilogram of body weight). On sternal puncture there were 78,000 leukocytes and 180 megakaryocytes per cubic millimeter of spinal fluid. Urinalysis gave negative results. Histologic examination showed scleroderma.

DISCUSSION

DR. EUGENE T. BERNSTEIN: This case presents the so-called white spot disease and shows all stages of development: the stage of edema; the second stage, showing redness, and so on. However, I think another diagnosis should be entertained, namely, scleropoikilodermae, the type described by Kaete Jaffe (*Arch. f. Dermat. u. Syph.* **159**:257, 1930). It is a spreading or generalized type of poikiloderma resulting in scleroderma and also involvement of the muscles.

DR. CHARLES WOLF: There is one point in the history which makes me feel that there must be some error, and that is the low sugar content of the blood. A patient with a blood sugar content of 60 mg. per hundred cubic centimeters is in a state of hypoinsulinism. For the sake of the record, therefore, I suggest that the blood sugar determination be repeated. It is extremely low for a patient who apparently is not suffering any discomfort.

DR. HERMAN GOODMAN: What is this man's occupation?

DR. HENRY D. NILES: This man is a mechanic in an aviation factory. The scleroderma started on his hands. He has done a lot of work with an electric riveting machine. Whether the vibration and trauma had anything to do with the development of this condition I don't know. As far as the blood sugar is concerned, that amount was recorded in the history. According to the standards at the New York Post-Graduate Medical School and Hospital, 60 mg. per hundred cubic centimeters is not so low; 65 mg. per hundred cubic centimeters is the average normal, with normal variations from 50 to 80 mg. However, 60 mg. would be low for the total blood sugar, the normal value of which ranges from 70 to 100 mg.

DR. CHARLES WOLF: The normal limits of the blood sugar are between 90 and 120 mg. per hundred cubic centimeters.

DR. MARION B. SULZBERGER: The variation in the values of blood sugar in normal persons depends on the different methods used for its determination.

DR. E. WILLIAM ABRAMOWITZ: I should like to suggest that an investigation be made for parathyroid disease. The patient may have a hyperparathyroidism.

DR. HENRY D. NILES: No investigation has been made for parathyroid disease.

I thought that there would not be much doubt about the diagnosis except, perhaps, for the possibility of poikilodermatomyositis, which was suggested, but I was expecting the impossible perhaps, that I might get some suggestions as to therapy. The disease has had a rapid course, and the patient's condition is already pathetic. He is an expert mechanic, and the disease is beginning to interfere with his work. At this rate he will not be able to work much longer. He has had no treatment yet. Besides the unusual dermatologic picture, I was also interested in the peculiar laboratory findings. He has polycythemia, which I do not think one would suspect from looking at him, and a high basal metabolic rate. The medical clinic is interested in the blood volume, which is much higher than normal. I believe that the prognosis is bad because of the rapid course.

DR. E. WILLIAM ABRAMOWITZ: Was determination of arsenic done?

DR. HERMAN GOODMAN: What significance does arsenic have?

DR. E. WILLIAM ABRAMOWITZ: Arsenic is one of the causes being put forward lately for this condition.

Localized Scleroderma; Lingua Geographica; Hypertrichosis; Keratosis Pilaris. Presented by DR. FRANK C. COMBES and DR. MAURICE J. COSTELLO.

J. W., a girl aged 8 years, has had the present condition for three years, since January 1937. The eruption is located on the postauricular region, the left side of the neck and the sternomastoid and inframandibular region. Since 1937

there has been progressive involvement of the postauricular region and the lower half of the ear, including the lobe. Recently the eruption has extended to the inframandibular region. The skin is thickened, hyperpigmented and depigmented, having a waxy hue and feel. Newer lesions are indicated by pinhead-sized to half-lentil-sized, sharply circumscribed, guttate lesions, which are now evident on the submental region. In addition, the child has lingua geographica and hypertrichosis. The mother claims that the hair on the body becomes less evident with changes in season. She states that the child was born with an excessive growth of hair on the scalp and the lower part of the sacral region. The bones of the body are normal. There is a longitudinal and transverse enlargement of the heart. There is bilateral hilar adenopathy, with numerous calcified foci at the roots of both lungs. A systolic murmur is heard at the apex of the heart. The mother states that the child had pica (eating cigaret ashes, sweaters and plaster from the walls). The blood count is normal. Chemical examination of the blood showed 94 mg. sugar, 10.4 mg. calcium, 5.5 mg. phosphorus, 10 mg. phosphatine and 166 mg. cholesterol per hundred cubic centimeters. Keratosis pilaris involving the posterolateral aspects of the extremities has been present from time to time.

DISCUSSION

DR. DAVID BLOOM: I presented this child a few years ago (ARCH. DERMAT. & SYPH. **38**:473 [Sept.] 1938) before this section. I notice that since then great improvement has taken place in the consistency of the skin behind the ear and of the ear itself. I believe that this improvement is spontaneous and independent of any therapy which the child has received.

DR. E. WILLIAM ABRAMOWITZ: An interesting point is that the child suffers from pica, eating substances such as cigaret ashes and plaster from the walls, which are known to contain arsenic and lead.

DR. MAURICE J. COSTELLO: In regard to treatment, this patient received padutin (a pancreatic extract) both by intramuscular injection and injection directly into the sclerodermatous area, as well as massage and infra-red therapy. Whether the improvement is due to the treatment or not I cannot say.

CHICAGO DERMATOLOGICAL SOCIETY

EDWARD A. OLIVER, M.D., *President*

HERBERT RATTNER, M.D., *Secretary*

Jan. 17, 1940

Lupus Vulgaris (Successfully Treated with Injections of Starch). Presented by DR. OLIVER S. ORMSBY and DR. ROBERT C. RANQUIST (by invitation).

Mrs. F. P., aged 77, is presented. Treatment was begun by us in 1920 and included phototherapy, cauterization with solid carbon dioxide, application of keratolytic agents and special diets, all of which only partially controlled the condition. At the present time the major portion of the eruption is on the left arm above the elbow. When first seen the patch was the size of a silver dollar and presented the usual appearance, being slightly elevated, scale covered and reddish brown. The margins showed distinct brown nodules, easily demonstrated on diascopic examination. The injections of starch were instituted on May 4, 1939 and have been repeated at variable intervals, usually of fourteen days. Each consisted of 0.2 cc. of a 15 per cent suspension of arrowroot starch in Ringer's solution. The starch was sterilized in 150 C. dry heat for one hour, as described

by Chambers and Grand (The Chemotactic Reaction of Leukocytes to Foreign Substances in Tissue Culture, *J. Cell. & Comp. Physiol.* **8**:1 [April] 1936). The injection is made intradermally into the nodule of lupus vulgaris.

DISCUSSION

DR. OLIVER S. ORMSBY: Any treatment offering good results in lupus vulgaris should be welcomed. This patient had made little progress toward recovery in eighteen years, whereas the starch injection treatment has largely cleared up the condition in ten months.

DR. ROBERT C. RANQUIST (by invitation): This treatment was undertaken because of the startling experience of R. L. Kile (ARCH. DERMAT. & SYPH. **39**:471 [March] 1939). The technic is as follows: About 0.2 cc. of a 15 per cent suspension of arrowroot starch in Ringer's solution is injected into each nodule about every two weeks. The explanation offered by Dr. Kile is that it was suggested to him because of the positive chemotactic action of starch on the leukocytes. The large grain starch molecules, such as those of corn starch or arrowroot starch, are best because they cannot be engulfed by a single leukocyte, and therefore an accumulation of leukocytes takes place at the site of injection. Eight months after beginning the treatment this patient's skin is about 80 per cent clear, after her having had the disease for sixty-seven years.

Pemphigus Limited to the Mucosa and Conjunctiva. Presented by DR. A. W. STILLIANS.

An American woman of at least 50 years said that since 1935 she had had frequent nosebleeds. In the fall of 1936 her throat became sore. In May 1937 she was seen to have erosions of the mouth, nose, pharynx and larynx which refused to heal under the usual treatment; some would heal and reappear, and others refused to heal. The ocular trouble was first noticed early in 1935. In 1937 her blood was tested and the Wassermann and Kahn reactions were found to be weakly positive. The Frei test gave a negative result. The urine was normal. Examination of the blood showed 80 per cent hemoglobin (Sahli method) and 5,500 leukocytes per cubic millimeter, with a differential count within normal limits. The blood pressure was 114 systolic and 70 diastolic. Between May 1937 and November 1938 the patient was given seventeen intravenous doses of an arsenical and twenty-five intramuscular injections of a bismuth compound. These and the potassium iodide always made her feel worse but caused no visible exacerbation of the lesions. In November 1938 two phytopharmacologic tests were reported as yielding indexes of 39 and 48 per cent respectively. Up to November 1938 the synechiae were limited to the external third of the lower lid. Recently the ocular condition has become much worse, although the lesions of the mouth are decidedly better. There had never been any blisters on her skin except those from trauma.

Examination reveals a well nourished woman whose left bulbar conjunctiva is covered by a milky film up to the limbus of the cornea; there are many adhesions between the bulbar conjunctiva and that of the whole lower lid. There is also considerable congestion of the conjunctiva. On the inner side of the left cheek is a red macule slightly eroded, and on the anterior surface of the uvula, a triangular erosion with slightly reddened borders. There are similar small erosions in the pharynx.

DISCUSSION

DR. PAUL A. O'LEARY, Rochester, Minn.; The term ocular pemphigus has also been used to describe contracting conjunctiva of this type, and I have believed for some time that the use of the term pemphigus for this disease was a misnomer. The patients rarely, if ever, present the cutaneous manifestations of common or vegetating pemphigus; neither does involvement of other mucous membrane surfaces develop. Conversely, this type of conjunctival lesion is not encountered

in the classic case of pemphigus. The disease has impressed me as a local infection rather than a systemic one, and continued search for organisms perhaps other than bacteria seems indicated.

DR. RICHARD S. WEISS, St. Louis: I have observed only 1 case in which the condition began with lesions on the conjunctiva and other lesions proceeded to develop on the body and proved to be pemphigus. I am inclined to agree with Dr. O'Leary.

DR. RUBEN NOMLAND, Iowa City: I have had the opportunity to observe 6 cases of ocular pemphigus, in 3 of which there were mucous membrane lesions of the mouth and in 2, involvement of the vulva, anus and umbilicus. The term ocular pemphigus is well known to ophthalmologists, and it is a syndrome that leads to blindness. It is probably different from the pemphigus vulgaris which the dermatologist sees, but ocular pemphigus with lesions of the mucous membranes approaches some of the more benign types of pemphigus vulgaris.

DR. OLIVER S. ORMSBY: This subject has come up before this society frequently in the past twenty-five years, and during all this time I have never seen a patient with pemphigus of the skin together with the so-called ocular pemphigus. I do not believe that what the ophthalmologists call ocular pemphigus is pemphigus from a dermatologic standpoint. I know, however, that it is a well defined entity. I think there is no connection between pemphigus and so-called ocular pemphigus.

Atrophoderma with Telangiectasia. Presented by DR. OLIVER S. ORMSBY.

M. S., aged 61, was first presented before this society in January 1928 (ARCH. DERMAT. & SYPH. **34**:724 [Oct.] 1936). The duration of the condition is now forty-seven years. At present the entire trunk is involved and shows a patchy, scaly, telangiectatic and atrophic condition. Psoriasiform patches are present on the knees and other areas. Telangiectasia and atrophy are most pronounced on the breast and on the extensor surfaces of the arms, buttocks and thighs. Histologic examination showed a picture compatible with the findings of idiopathic atrophy (Herxheimer). During twelve years' observation and treatment much improvement has occurred on the face and to a more moderate extent on the trunk.

DISCUSSION

DR. UDO J. WILE, Ann Arbor, Mich.: I recall distinctly having seen this patient before. Were it not for the fact that the disease had been present for forty-seven years, I should be suspicious that mycosis fungoides was developing. The circumscribed lesions on the legs and thighs, together with the microscopic observation of a sharply circumscribed infiltrate in the upper layer of the corium, certainly suggest this possibility. The concept that so-called poikiloderma may be associated with or part of a malignant condition would readily tie up with the idea of beginning mycosis fungoides.

DR. H. E. MICHELSON, Minneapolis: The microscopic section to me is interesting because in spite of the length of time the patient has had the condition there is still a decided infiltrate. I think the condition is acrodermatitis chronica atrophicans.

DR. PAUL A. O'LEARY, Rochester, Minn.: I have had the opportunity of seeing this patient at previous meetings of this society, and on each occasion the relation of poikiloderma atrophicans vasculare with mycosis fungoides is brought to mind. Dr. Otto Foerster called attention to the association of these two conditions more than ten years ago. Some of my colleagues believe that my concept of poikiloderma is not concrete; however, I have observed this syndrome in association not only with mycosis fungoides but also with chronic lupus erythematosus disseminatus and with dermatomyositis, as well as in its idiopathic form. In other words, the cutaneous picture of atrophy and telangiectasia, which is called poikiloderma atrophicans vasculare, either localized or disseminated, may

appear in conjunction with or subsequent to several diseases. So I like to consider poikiloderma atrophicans vasculare as the result of injury to the cutaneous vascular structure by various noxae. I believe a somewhat broader view of poikiloderma should be maintained than that held in the past, and the condition should be considered the end result of the insult of various agents rather than a single entity.

DR. EDWARD A. OLIVER: In the case I presented and later reported of mycosis fungoides with poikiloderma-like symptoms, Dr. Nomland first made the diagnosis. It was first presented as a case of acrodermatitis with poikilodermic symptoms.

DR. M. OPPENHEIM (by invitation): In a monograph on atrophy of the skin (Finger, E. A., and Oppenheim, M.: Die Hautatrophicen, Vienna, Franz Deuticke, 1910) and in my article in Jadassohn's handbook on atrophy of the skin (Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 8, pt. 2) I expressed the opinion that Jacobi's "Poikiloderma" (*Verhandl. d. deutsch. dermat. Gesellsch* **9**: 321, 1907) is only a special form of dermatitis atrophicans. Other cases of poikiloderma are only endings of various cutaneous diseases, as the cases of Petges and Cléjat, which are of dermatomyositis, and those of Civatte and Müller, which are of lupus erythematosus. I presented a case before the Vienna Dermatological Society, in which poikiloderma was the prestage of mycosis fungoides. Lichen planus, psoriasis vulgaris and other chronic cutaneous diseases can cause poikiloderma; it may be caused by treatment too. I believe that the presented case is a combination of psoriasis vulgaris with dermatitis or acrodermatitis atrophicans. The clinical findings are in some areas typical for psoriasis vulgaris and in other areas typical for dermatitis atrophicans. The histologic observations are not evidence of mycosis fungoides in the prefungoid stage, because there is no polymorphism of cells. I did not see the conditions of the elastic fibers. If they are absent, then I guess the condition is a combination of dermatitis atrophicans and psoriasis vulgaris.

DR. OLIVER S. ORMSBY: I do not think this condition is poikiloderma of Jacobi. In poikiloderma there is always more pigmentation than is present in this case. Some of the lesions here are psoriasiform, but the condition is not psoriasis. These are of comparatively recent origin. The peculiar effect, resembling a roentgen ray burn (healed radiodermatitis), that occurs in poikiloderma is not seen here. The disease is of forty-seven years' duration but has had little effect on the general health. The lesions on the face have practically cleared. The extreme itching is not characteristic of any of the diseases under discussion. The histologic picture is that of idiopathic atrophy. The discussions in this case in the past have centered around idiopathic atrophy, poikiloderma of Jacobi, lupus erythematosus and psoriasis.

Atypical Lepra. Presented by DR. S. W. BECKER and DR. M. E. OBERMAYER.

The patient was presented at the November 1939 meeting of the Chicago Dermatological Society (ARCH. DERMAT. & SYPH. **41**:1151 [June] 1940), with a tentative diagnosis of histiocytoma.

The lesions were inoculated with 1 per cent saccharated iron oxide, which was ingested by a few histiocytes but was not taken up by the cells in the massive infiltrate. In sections stained with carbolfuchsin, some but not all of the infiltrating cells were seen to contain a large number of acid-fast bacilli, singly and in groups. Some of the cells contained a large mass of acid-fast material of indefinite form.

On the basis of these observations the diagnosis of lepra has been made.

DISCUSSION

DR. UDO J. WILE, Ann Arbor, Mich.: While several of the members were examining this patient, I went over various parts of her body with a pin and found that she is completely anesthetic over the entire front and lower extremities. I cannot say why this condition is anything more than the usual leprosy of the mixed type.

DR. H. M. HEDGE: I understood Dr. Becker to say there was no anesthesia.

DR. S. W. BECKER: This woman has never had a neurologic examination to my knowledge. I did not know that she had anesthetic areas.

NOTE.—Subsequent neurologic examination revealed hypalgesia over the right side of the face and the upper part of the left side of her back. The neurologic consultant stated that the findings suggested involvement of cutaneous sensory nerves but were not convincing.

DR. UDO J. WILE: I stuck the pin in both arms 1/16 inch (0.16 cm.).

DR. S. W. BECKER: Do you consider this condition an anesthetic type of lepra?

DR. UDO J. WILE: I consider it a mixed type.

DR FREDERICK R. SCHMIDT: I can easily appreciate Dr. Becker's quandary, because in 1938 a patient with lepra was presented here whom I had treated for six months for urticaria. I then found lepra bacilli in abundance in November 1938, and she was presented later before the society as definitely having leprosy. There was no indication of that six months previously.

DR. DAVID LIEBERTHAL: The clinical symptoms are in no respect typical of this disease, and I believe that the painstaking work-up, including the biopsy, made the correct diagnosis possible.

A Case for Diagnosis. (Dermatitis Herpetiformis? Pemphigus?). Presented by DR. THEODORE CORNBLEET and DR. HERBERT RATTNER.

A. A., a 73 year old Scotchman, states that he has never had any previous cutaneous trouble. He was in good health until May 1939, when one week after moving a mildly pruritic bullous eruption developed over the sternum. He broke the blisters and applied sulfur and oil to the denuded areas. New crops of bullae appeared on the arms, forearms and thighs, and when the old lesions healed new ones developed. He has never been entirely free of any lesions since the onset but has never noticed any in the mouth.

The patient's chief complaints on admission to the hospital, on Dec. 7, 1939, were itching of the thighs and trunk and constipation.

There is no history of any similar disease in the family.

Examination of the skin reveals bullae on the extensor surface of the arms and on the flexor surfaces of the upper parts of the forearms, the thighs and the legs, on a nonerythematous base, somewhat grouped and in different degrees of distention, with a translucent amber fluid. Several of the bullae contain a milky fluid. In the same areas are denuded erythematous lesions of ruptured bullae with some overhanging epidermis and excoriations. On the sides of the trunk and abdomen a light pinkish, follicular, papular eruption is present, which was erythematous several days ago but is fading now. Physical examination, apart from the skin, gave essentially negative results. The skin of the back is erythematous and moist because she has been lying on her back. Nikolsky's sign is not present.

Urinalysis gave negative results. The Kahn reaction of the blood was negative. A blood count showed 89 per cent hemoglobin and 4,800,000 erythrocytes and 21,700 leukocytes per cubic millimeter, with a differential count of 68 per cent polymorphonuclear leukocytes, 20 per cent eosinophils, 1 per cent plasma cells, 7 per cent lymphocytes and 4 per cent monocytes. Chemical examination of the blood showed normal amounts of nonprotein nitrogen, creatinine and sugar.

DISCUSSION

DR. RICHARD S. WEISS, St. Louis: I got the impression that this patient has chronic pemphigus. I feel that as time goes on this will become more evident.

DR. M. H. EBERT: I agree with the presenters that this condition, which at first appeared to be dermatitis herpetiformis, may terminate in pemphigus, but I think at the present time it is dermatitis herpetiformis.

DR. THEODORE CORNBLEET: I felt in the beginning that the distribution of this man's eruption was definitely that of dermatitis herpetiformis, and several of the physicians who saw him feel that that is still the proper diagnosis. There is no question that he has lost considerable ground since he has been hospitalized. I think that there is a lot of room for Dr. Weiss's opinion that this is a case of pemphigus. I believe, however, that at the present time it is impossible to say definitely whether it is pemphigus or Duhring's disease and that it is one of those cases that requires the passage of time before a definite diagnosis can be made.

Recklinghausen's Disease with Demonstration of Nerve Fibers in a Tumor. Presented by DR. M. H. EBERT.

H. M., a woman aged 27, presents an extensive eruption which she first noticed at the age of 21. She has 3 brothers and 3 sisters, and no others in the family have a similar trouble. Her intelligence quotient is about normal. The patient is rather undernourished and has a definitely asymmetric face. The cutaneous lesions are most numerous on the trunk and are of four general types: (1) numerous bluish, slightly raised, compressible tumors which give the impression of hibernation on pressure; (2) numerous sessile and pedunculated fibrous tumors varying from scarcely visible growths to bean-sized ones, the color of the normal skin; (3) several café-au-lait macules, and a (4) few walnut-sized, flabby tumors.

The histologic sections demonstrated were taken from a match head–sized fibrous tumor of the second type. Part of the tumor was fixed in Bouin solution and stained with Masson's trichrome stain. Part was impregnated with silver, according to a modified Cajal technic. The sections stained with Masson's trichrome stain show the usual loose fibrillary structure, with numerous nuclei. There are many thin-walled blood vessels and lymph spaces. In the silver-impregnated section there are several cross sections and longitudinal sections of nerve fibers. In the center of the section the nuclei in the reticulum are particularly numerous, and there are many nerve fibrils running between them.

DR. M. H. EBERT: The case of Recklinghausen's neurofibromatosis was presented to demonstrate the involvement of the nerve fibers, by means of a modified J. Gay Prieto technic (*Bull. Soc. franç. de dermat. et syph.* **42**:1069, 1935) to visualize the finer nerve fibrils with silver nitrate. Von Recklinghausen himself thought the disease consisted of a proliferation of the connective tissue around the intact nerves. Verocay (*Beitr. z. path. Anat. u. z. allg. Path.* **48**:1, 1910) years later came to the conclusion that the condition should properly be called a neurinomatosis, because he stated the belief that it was due to the proliferation of the undifferentiated ectodermal cells, which in the course of time would normally develop into Schwann's cells. The section shown today was taken from a small fibroma-like tumor. At the periphery can be seen many normal nerve fibrils, but in the center of the tumor, where the reticulum contains the most nuclei, a nerve fiber is visible which has been much distended, so that the neural axons project out of the neurilemma and run between the nuclei of the surrounding reticulum. This multinucleated reticulum is probably a proliferation of embryonic Schwann cells.

Epidermolysis Bullosa Dystrophica. Presented by DR. TIBOR BENEDEK (by invitation).

The patient is a 35 year old man of Irish descent. His parents have been dead for a long time; 5 brothers are living and well. According to the patient's own story, no one in the family has had any cutaneous disease. His present eruption started about twelve years ago. The skin turned purplish on both elbows and knees and became thinner. A few years after the onset blisters appeared within the thinned and purplish areas after bruising the skin.

He was admitted to Mandel Clinic, Michael Reese Hospital, and shows a purplish, atrophic, cigaret-paper-like scarring on both elbows and knees, forearms

and shins. On the left elbow there is a large bulla about 8 by 2 cm., which is tense and filled with clear serum. Around this are numerous blisters, 3 to 5 mm. in diameter, tense or flaccid or already ruptured, showing a purplish red, oozing or crusted surface. The left shin shows within the purplish, atrophic areas numerous bullae, 5 to 10 mm. in diameter, and further eroded or crusted lesions. Both shins reveal slight pigmentation, hemorrhages and telangiectasis. On the back of the right calf, in an area 12 cm. in length, there are partly isolated, partly confluent purplish atrophic lesions. Similar lesions are present on the left calf in smaller number. The skin of both buttocks shows an extensive white, macular, atrophic scarring. On the right buttock there are two larger areas, one 6 by 3 cm. and the other smaller. On both shoulders and scattered also on the upper part of the back are similar lesions 10 to 15 mm. in diameter.

As accompanying and complicating symptoms there are numerous white macular, atrophic lesions on the chest, the abdomen and along the vertebral column down to the sacrum; they are round, oval or irregular in shape, 5 to 25 mm. in diameter. Milium bodies are present, especially on the forearms.

The nails of all the fingers and toes are atrophic, being replaced by a few layers of dirty brownish, horny masses. The hair covering is normal all over the body. The mucous membranes have never shown blister formation, according to the patient. Nikolsky's phenomenon could not be elicited.

NOTE.—The Wassermann and Kahn reactions of the blood were negative. Tests showed no hematoporphyrin in the urine. Examination of the blood showed 75 per cent hemoglobin, 4,800,000 red cells and 12,100 white cells per cubic millimeter, with a differential count of 49 per cent neutrophils, 1 per cent eosinophils, 47 per cent lymphocytes and 3 per cent monocytes.

DISCUSSION

DR. A. W. STILLIANS: It is a little puzzling as to how to classify this case, because of the ability of the skin to produce bullae only in the atrophic areas. There was a history of atrophy that lasted for several years before the bullae appeared.

Arsenical Keratoses. Presented by DR. F. E. SENEAR and DR. W. K. FORD (by invitation), Rockford, Ill.

Mrs. P. S., aged 28, was first seen on Dec. 14, 1939, and complained of horny lesions on the palms and soles of three years' duration. She states that her husband and 7 year old daughter had similar lesions on the palms and soles. Her husband's eruption began three years ago, and her daughter's appeared about one year ago. Close questioning failed to reveal any history of ingestion of arsenic or of contact with sprays containing arsenic. The patient was instructed to return with her husband and daughter, which she did on Jan. 4, 1940. At this time her husband stated that there had been a can of powder (used for spraying golf greens) in the basement of their home when they moved into it five years previously; the bottom of the can had gradually rusted away, and some of the contents leaked into their well from time to time, giving the water an acid taste.

The eruptions are strongly suggestive of arsenical keratoses, and the difference in degree of the eruption may possibly be accounted for by the variable quantities of water taken by each patient. Another daughter, aged 3 years, does not present any eruption.

DISCUSSION

DR. LOUIS A. BRUNSTING, Rochester, Minn.: The presence of keratoses in father, mother and child is remarkable. No doubt these changes are a quantitative response to arsenic rather than an idiosyncratic reaction, such as is suggested when keratoses appear in association with asthma, psoriasis or dermatitis herpetiformis. The investigative work in this case is commendable.

DR. OLIVER S. ORMSBY: All my associates recognized in this patient this afternoon a similarity to one presented a few years ago in whom an arsenical eruption was produced by drinking well water. The patient came from Mexico where he had lived for twenty-five years. He presented a large number of keratoses and several epitheliomas. A careful search was immediately made for arsenic. He stated he had never taken any drugs. Examination of the well water he drank in Mexico showed that it contained a considerable percentage of arsenic. The patient was of interest on account of the extensive distribution and large number of lesions. He was the only member of his family affected.

DR. W. K. FORD (by invitation), Rockford, Ill.: There is just one point further that the mother gave as she left the hospital. About a year and a half ago she was in an automobile accident and was confined to the hospital for two and one-half months, and during that time the eruption on the palms and hands cleared up; after her return home there was a recurrence of the eruption.

Kaposi's Sarcoma. Presented by DR. S. J. ZAKON (by invitation).

D. R., a Jewish man aged 63, was first seen in 1932. At that time he presented a dusky and sharply outlined, infiltrated plaque on the dorsum of the right hand. Histologic examination of the lesion was made, and a diagnosis of Kaposi's sarcoma made. The patient did not return for treatment until October 1939, when he complained of progressing deafness, edema of the legs, swelling of the scrotum and growths in the mouth. Physical examination revealed a generalized, fairly symmetric, discrete eruption involving the scalp, face, chest, back, extremities, roof of the mouth, left tonsil and right auditory canal. The eruption consisted of nodules and plaques, red to plum colored, and boardlike verrucous infiltrations over the dorsa of the feet and ankles. The nodules on the knees appeared to be pedunculated. There were no palpable glands. The lesions of the soft palate and the left tonsil were elevated nodes or tumors, soft and plum colored.

A blood count in October 1939 showed 70 per cent hemoglobin, and 3,730,000 erythrocytes and 6,400 leukocytes per cubic millimeter, with a differential count of 86 per cent polymorphonuclear leukocytes, 8 per cent small lymphocytes, 4 per cent large lymphocytes and 2 per cent monocytes. The blood pressure was 120 systolic and 68 diastolic.

Since October treatment has consisted of solution of potassium arsenite U. S. P. given internally and unfiltered roentgen rays. There is beginning involution of some of the lesions. Histologic examination of lesions from the tonsils and skin showed findings compatible with those usually seen in Kaposi's sarcoma.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis: I thought this case was a remarkable example of Kaposi's sarcoma, but on looking at the patient's fingers, I was struck by the fact that there is a similarity between Kaposi's sarcoma and sarcoidosis; the relation is not definite, but tissues of the same type are prone to react the one in a benign manner and the other in a much more severe manner.

DR. S. W. BECKER: I should like to differ with Dr. Michelson because sarcoid involves reticuloendotheliosis, representing a reaction on the part of the histiocytes to some agent which is often known, such as the tubercle bacillus or one of the aberrant forms of the tubercle bacillus. With Kaposi's sarcoma, on the other hand, there is multiplication of cells, multicentric in origin, throughout the body, the stimulus for which multiplication is not known but which results in the formation of a unique type of cell, the fusiform cell. Dr. Thatcher and I had occasion to study these cells in tissue cultures (Becker, S. W., and Thatcher, H. W.: Multiple Idiopathic Hemorrhagic Sarcoma of Kaposi, *J. Invest. Dermat.* **1**:379, 1938). In these cultures there were many histiocytes which differed greatly from the fusiform cells. The latter were not fibroblasts, and they did not act as malignant cells do. I think that in Kaposi's sarcoma there is a unique type of cell reaction of the embryonic cells. The lymphocytoid cells of Marchand are stimu-

lated by some unknown agent to produce a benign neoplasm. I believe Kaposi's sarcoma is a benign neoplasm. In some instances it goes on to malignant hyperplasia, just as myofibroma of the uterus occasionally goes on to the formation of sarcoma. I do not see how the two conditions, sarcoid and Kaposi's sarcoma, are related.

DR. DAVID LIEBERTHAL: The clinical manifestations justify the diagnosis offered. As multiple hemorrhagic sarcoma lasts only a few years and as a rule causes impairment of the general health of the patient sooner or later after the onset of the disease and terminates fatally, Dr. Zakon's case may be considered an unusual one, the condition having lasted for about twenty-five years, during which the patient has been enjoying good health.

DR. H. M. HEDGE: In 1920 I presented a case of Kaposi's tumor before the society. The patient is still alive, and I saw him a short time ago.

Avitaminosis. Presented by DR. DAVID V. OMENS.

L. Y., a Negress aged 35, has been sick for three weeks. She presents an acute and diffuse inflammation of the tissues of the mouth, pharynx, larynx and vagina, with superficial denudation of the epithelium with remnants of the epithelium still intact. She gives a history of having partaken of considerable alcohol with little or no food except some hamburger meat occasionally for some time previous to this condition.

The Wassermann reaction was negative. The urine and the blood sugar content were normal. Cultures for the Klebs-Löffler bacillus were negative. Smears from the mouth revealed Vincent's bacilli, diphtheroid bacilli, staphylococci and streptococci. A vaginal smear was negative for Vincent organisms and monilias. Examination of the blood showed 96 per cent hemoglobin, 5,270,000 erythrocytes and 11,800 leukocytes per cubic millimeter, with a differential count of 75 per cent polymorphonuclear leukocytes, 2 per cent eosinophils, 10 per cent lymphocytes and 13 per cent monocytes. Chemical examination of the blood showed 136 mg. sugar, 41 mg. nonprotein nitrogen and 2.4 mg. creatinine per hundred cubic centimeters.

DISCUSSION

DR. J. R. DRIVER (by invitation), Cleveland: I thought the case was a typical one of pellagra. Treatment with nicotinic acid would probably be specific.

DR. J. GARDNER HOPKINS (by invitation), New York: The patient's mouth is filled with ulcerated lesions that look as though they were ruptured bullae. I think pemphigus must be considered.

DR. HERBERT RATTNER: I thought that the case was one of pellagra. At the Cook County Hospital cases of pellagra are occasionally encountered with symptoms in the mouth only. And it has been pointed out that one is likely to recover thrush organisms from the mouth of a pellagrin. At any rate, conditions such as the one presented today clear up rapidly when treated with nicotinic acid.

A Case for Diagnosis (Macular Atrophy?). Presented by DR. F. E. SENEAR and DR. W. K. FORD (by invitation), Rockford, Ill.

A. H., a white girl aged 10 years, is presented. Her mother first noticed the eruption six months ago in the interscapular area. She described it as resembling tiny white blisters that seemed to become solid and grow in size. New lesions appeared from time to time. There were no subjective symptoms. The eruption consisted of discrete round and slightly elevated white macular lesions which were present in the interscapular area, left axillary area and flank, lumbar area and anterior surface of the right thigh.

The patient had whooping cough at the age of 4 years, pleurisy and otitis media at the age of 5 years and varicella followed immediately by measles at the age of 9 years. The eruption did not appear for many months after the last illness.

The blood count showed 81 per cent hemoglobin and 4,230,000 erythrocytes and 7,700 leukocytes per cubic millimeter, with a differential count of 45 per cent poly-

morphonuclear leukocytes, 47 per cent lymphocytes and 8 per cent monocytes. The Kahn reaction was negative, and the urine was normal.

A lesion in the lumbar area was removed for histologic examination. The epidermis was flattened and showed slight intracellular edema. The corium was relatively avascular, with thickening of the collagen fibers, which stained poorly. The elastic fibers were thin and fragmented in the upper part of the corium.

DISCUSSION

DR. OLIVER S. ORMSBY: It is rather unusual for macular atrophy of that type to occur in a young child. I thought of morphoea guttata, and that disease has to be considered. However, the lesions are white, macular and atrophic, which might place it as macular atrophy.

DR. M. R. CARO: In Dr. Ford's case the histologic slide showed that the epidermis was flattened, but there was no complete atrophy. The collagen fibers were thickened and hyalinized. Histologically the condition fits in with the diagnosis of white spot disease much better than with macular atrophy.

DR. S. W. BECKER: I agree with Dr. Caro that these lesions have a distinctly sclerodermatous appearance. I believe that some of them at least should be placed in the category of scleroderma and perhaps white spot disease, although some of the others may have gone on to atrophy.

DR. DAVID LIEBERTHAL: I believe that this case is one of macular atrophy of the skin. It would be desirable to ascertain the family and clinical history, which might be helpful in the interpretation of the case. I have seen and demonstrated before this society some examples which developed on the basis of late papular syphilid.

Macular Atrophy (Schwenninger and Buzzi Type). Presented by DR. F. E. SENEAR and DR. IRENE NEUHAUSER (by invitation).

M. B., a white girl aged 14, is presented with lesions on the trunk and right arm of many years' duration. She had measles during infancy, which was followed by the appearance of lesions on the trunk. From time to time until the present new lesions have appeared.

The patient has a number of coin-sized, oval and elongated atrophic lesions on the back and the right arm, with the long axis showing a tendency to follow the lines of cleavage. On the lower part of the abdomen there is an irregular, palm-sized area of hyperpigmentation. On the extensor surface of the right arm there are several slightly erythematous, elevated lesions of similar shape and size, which have a soft, doughy consistency on palpation. The atrophic lesions are covered with cigaret-paper-like scars and have a slight tendency toward herniation.

At the time these lesions developed, changes were also noticed in the right eye. The right bulb is slightly enlarged. The pupil is contracted but reacts to light and in accommodation. At present the patient is only able to distinguish light and darkness. Ophthalmoscopic examination revealed atrophy of the optic nerve. The corneal measurements are greater than normal, and the tension of the eye is increased.

A biopsy was not permitted.

DISCUSSION

DR. M. OPPENHEIM (by invitation): The cases of macular atrophy described by Jadassohn are characteristic. The condition starts as little red spots which become atrophic, with cigaret-paper-like surface. In the last stage there is a hernia-like prominence. Histologically, this hernia-like stage is characterized by fatty tissue in higher layers of the skin than normal. It is a fatty tissue growing in vacuo, substituting the degenerated and diminished connective tissue and elastic fibers of the cutis. The macular atrophy of the Schwenninger-Buzzi type is not a real cutaneous atrophy; it is due to the resorption of the fibromas. Therefore, on palpation one gets the impression, as in cases of atrophia maculosa, of a hole in

the skin. In acrodermatitis trophicans, as the first change histologically is an absence of elastic fibers, they cannot be stained. The reason is a constitutional weakness of the elastic fibers, which is also found in striae gravidarum. For instance, one sees sometimes a pregnant multipara with no striae, whereas sometimes after an abortion striae distensae appear. This girl presents an interesting example of Jadassohn's disease. The girl shown by Dr. Ford had scleroderma, in which the lesions always remain the same size.

A Case for Diagnosis (Fibrosarcoma of the Shoulder?). Presented by Dr. Edward A. Oliver.

The patient, a Negro aged 50, had a keloid (?) growth removed from the right shoulder in 1932. In March 1935 he was in an automobile accident, at which time he received lacerations of the right shoulder, and the old keloid scar was ruptured. Since then the scar tissue in the areas of multiple lacerations has never healed entirely, being tender all the time and draining occasionally.

General physical examination revealed nothing of importance.

The urine showed a trace of albumin but was otherwise normal. Examination of the blood showed 3,800,000 erythrocytes and 10,000 leukocytes per cubic millimeter, and the hemoglobin was 70 to 75 per cent. The Wassermann and Kahn reactions of the blood were negative. A smear from the lesion showed gram-positive cocci in chains and in irregular groups; no fungus was found.

On Jan. 12, 1940, a blood count showed 3,220,000 erythrocytes and 9,000 leukocytes per cubic millimeter, with a differential count of 78 per cent neutrophils (toxic), 20 per cent lymphocytes and 2 per cent eosinophils; nucleated red cells were present. Histologic examination showed fibrosarcoma of low grade malignancy.

DISCUSSION

Dr. Udo J. Wile, Ann Arbor, Mich.: I cannot reconcile this case and a diagnosis of fibrosarcoma. If a nevus were included in the original keloid, the present condition can well be a melanoblastoma.

Dr. Edward A. Oliver: I presented the patient with the diagnosis that the pathologist at the Veterans Administration Facility at Hines, Ill., made, with an interrogation mark, because I was surprised to see the pathologic diagnosis. When I first saw him I thought of the possibility of fibrosarcoma protuberans, as reported by Dr. Andrews some years ago. I also thought of neurosarcoma, though there was little pain.

Dr. Udo J. Wile: Fibrosarcoma is ordinarily metastatic.

Dr. Edward A. Oliver: The condition is much more malignant than it appears. I showed here some years ago a young man with a lesion on his back, who died about nine months later.

Dr. J. R. Driver (by invitation), Cleveland: I thought the lesion looked more like fibrosarcoma. There was ulceration present.

Dr. F. E. Senear: There was much in this eruption suggestive of dermatofibrosarcoma protuberans, since in that condition the lesions often begin with the development of hard cutaneous infiltrate, with later development of the elevated lesions. When the elevated lesions first appear they are likewise often firm, but as the surface becomes eroded they tend to become soft, and such softening is present in some of the lesions here. I have, however, never observed a case of progressive and recurrent fibrosarcoma in which ulceration of the excavation type present in this case had developed.

Myelogenous Leukemia. Presented by Dr. F. E. Senear.

A man aged 44 was well until the fall of 1939, when he complained of fleeting pains in his face. Shortly after this nodules began to develop on the trunk; the face became similarly affected a short time later, and the lips, especially the upper

one, became enlarged. He also complained of soreness of the mouth, which made eating difficult. When he entered the hospital his face showed a typical leonine aspect with numerous large firm red nodules, especially in the supraorbital region. The upper lip was so grossly swollen that it overlapped the lower lip. The skin of the trunk was covered with a great number of firm red elevated nodules varying in diameter from 1 to 3 cm. These were freely movable with the skin and painless. The hard palate showed an extensive ulceration covered with a foul grayish, easily removable membranous slough, and there was severe gingivitis. The posterior cervical, the left supraclavicular and the axillary glands were enlarged. The spleen was enlarged, extending 3 fingerbreadths beneath the costal margin, while the edge of the liver was palpable 2 fingerbreadths beneath the costal margin.

The Wassermann and Kahn reactions were negative. Examination of the blood showed 4,100,000 red cells and 130,000 leukocytes per cubic millimeter, 60,000 platelets, hematocrit (R) 35 per cent and hematocrit (W) 7 per cent. A differential count showed 3 per cent myeloblasts and promyelocytes, 7 per cent neutrophilic myelocytes, 9 per cent neutrophilic metamyelocytes, 16 per cent stab forms, 57 per cent polymorphonuclear neutrophils, 2 per cent eosinophils, 1 per cent basophils, 2 per cent lymphocytes and 3 per cent monocytes.

Aspiration of sternal marrow was performed, and the results of the examination of the blood and bone marrow led to a diagnosis of myelogenous leukemia by the hematologists.

DISCUSSION

Dr. F. W. Lynch, St. Paul: The eruption is much more extensive than is usual with myelogenous leukemia. Reports of myelogenous leukaemia cutis are more common in recent years, suggesting that this condition may not be as rare as it was once thought but that hematologic study was then inaccurate.

Dr. J. Gardner Hopkins (by invitation), New York: I reviewed the reports of myelogenous leukemia of the skin some years ago, and it appeared that all the cases were of atypical leukemia and many, if not all, could be interpreted as monocytic rather than myelogenous leukemia. Of course, the patients did not have enlarged spleen and liver as this man has; neither did they have the same type of cutaneous lesion. I should be interested to know whether the condition was regarded as myelogenous leukemia or as one of the myeloblastic leukemias, about the nature of which there is some argument. This is a most interesting and, I believe, an extremely rare case.

Dr. Udo J. Wile, Ann Arbor, Mich.: I have had the opportunity to observe an unusually large number of cases of cutaneous leukemia at the Simpson Memorial Institute at the University of Michigan, an institute founded for the study of diseases of the blood. Experience there has shown that nodules which occasionally precede the other symptoms of lymphatic leukemia occur on the body. Such lesions and infiltrates are far more common in lymphatic leukemia than in the myeloid type. This is with due regard to the fact that lymphatic leukemia is more common.

In myelogenous leukemia the usual form of lesions are hemorrhagic, particularly on the extremities and in the mucous membranes.

When nodules occur in myelogenous leukemia, they have a predilection for the head and face and closely resemble the lesions of nodular leprosy.

Dr. Senear's case presents an admirable example of this similarity. The lesions on the skin are like those of nodular leprosy. The hemorrhagic lesions in the mouth are characteristic of the ordinary lesions which occur, particularly near the end of leprosy. If one were to examine microscopically the uninvolved portions of the skin at this stage, I am sure that one would find a cutis infiltrated with cells of the same type as those occurring in the tumor.

Dr. Richard S. Weiss, St. Louis: I have observed only 1 case, which I can recall, of proved myelogenous leukemia of the skin. It was one Dr. Engman Sr. had some twenty years ago. The patient had three rather large nodules on the face. They developed before the blood count became abnormal. In the course of two or three months' observation the blood count showed a typical myelogenous

leukemia. I have had a large number of cases of leukemia involving the skin, but myelogenous leukemia seems to be extraordinarily rare. The patient presented today shows many more lesions than are usually described in myelogenous leukemia of the skin.

DR. F. E. SENEAR: Dr. Hopkins has called attention to the fact that pictures of this type are rare in association with myelogenous leukemia, and he asks whether or not the condition may be one of monocytic type. I can say only that the hematology department at the Research and Educational Hospital, University of Illinois, has done a great deal of work on the monocytic type, and in this case the blood picture is reported to be that of a myelogenous type.

A Case for Diagnosis (Lymphosarcoma?). Presented by DR. EDWARD A. OLIVER and DR. LEE KERRIGAN (by invitation).

Mrs. G. S., a white woman aged 62, was first seen by me on Sept. 29, 1936. At that time she complained of a painful tender lesion on the upper alveolar ridge on the left side and a similar lesion on the right side of the soft palate. Both lesions were dark bluish red and had the appearance of lesions of multiform erythema. On being questioned she revealed that she took a pink cathartic pill every night, and it was thought that the pills might contain phenolphthalein. She was given an antiseptic mouth wash and instructed to stop taking the tablets. She improved rapidly, but two months later had a recurrence of the same lesions in the same locations. Five months later the lesion on the right side of the palate was more decided than ever, and a histologic examination showed granuloma. The large lesions finally disappeared, but all during 1937 and 1938 she had continual flare-ups of lesions on both sides of the gums in the front of her mouth. Certain foods seemed to bother her, and she had the material in her plates changed.

By October 1938, two years after I had first seen her, her mouth was not troubling her, but she complained of a "sleepy" feeling in her eyes, and inspection showed a pronounced ptosis of both upper eyelids.

The patient was not seen again for five months, and in February 1939 she returned with severe ptosis of both upper eyelids, together with lipoma-like tumors on both sides of the head in the parietal regions. The Wassermann and Kahn reactions were negative. Examination of the blood showed 4,820,000 erythrocytes and 5,750 leukocytes per cubic millimeter and 91 per cent hemoglobin, with a differential count of 33 per cent small lymphocytes, 6 per cent large mononuclear leukocytes, 57 per cent neutrophils, 1 per cent eosinophils and 3 per cent basophils.

On June 9, 1939, there was a violaceous discoloration of practically the entire top of the head; there was more involvement in the left parietal region than elsewhere, and there were decided alopecia and telangiectasia, with some crusting. A tumor had been removed from the left parietal region, and in the right parietal region another pigeon-egg-like tumor was present. There was still definite ptosis of both upper eyelids. In the right submaxillary region there was a large tumor the size of a pigeon egg. The one that had been present on the left side had been excised. There was moderate enlargement of the axillary nodes.

Histologic examination was made in South Bend, Ind. The following tissues were examined: a small portion of skin from the left parietal region, tissue from under the scalp, an axillary lymph node and a tumor from the submaxillary region. A diagnosis of lymphosarcoma was made.

Since June her treatment has consisted of filtered roentgen ray therapy, as follows:

June 30, 1 skin unit, filtered through 1 mm. aluminum to each side of neck

July 21, 1 skin unit, filtered through 1 mm. aluminum to right side of neck and left side of scalp

September 1, 1 skin unit, filtered through 1 mm. aluminum, to right side of scalp

September 22, ½ skin unit between the eyes and to the right side of scalp

November 15, ½ skin unit to swellings in both parietal regions

On July 13 examination of the blood showed 88 per cent hemoglobin and 4,200,000 erythrocytes and 6,100 leukocytes per cubic millimeter, with a differential count of 73 per cent polymorphonuclear leukocytes, 24 per cent small lymphocytes and 3 per cent large mononuclears.

The patient has gained 12 pounds (5.4 Kg.) in weight recently and looks and feels well. She has had wens on her scalp for years, and five of them have been removed at intervals.

DISCUSSION

DR. F. E. SENEAR: One of the early lesions was of a soft, projecting fungoid type. With regard to the condition of the scalp, I think it is worth emphasizing that this patient had definite telangiectasia as a result of the primary disease of the scalp and that there has been no accentuation of the telangiectasia following the radium therapy.

DR. EDWARD A. OLIVER: I thought this case was fairly interesting; I had never observed one like it. The disappearance of the tumor under small doses of filtered roentgen therapy suggested that possibly the lesion was lymphosarcomatous. The spleen and liver were not palpable when I examined her this morning. Her blood count remains about the same.

A Case for Diagnosis (Dermatitis Herpetiformis in a Child?). Presented by DR. F. E. SENEAR.

B. S., a girl aged 5 years, noticed a number of vesicles and bullae between the toes which developed in January 1939. Within two weeks similar lesions had appeared on the feet, legs and thighs; within a month the trunk and face were profusely affected and there was a high fever. The child was admitted to a hospital at the time, and a diagnosis of impetigo was made. By October the eruption on the body had cleared, but the lower extremities were still affected. The diagnosis at this time was changed to dermatitis herpetiformis. No details as to the treatments employed were available.

The patient was admitted to the Research and Educational Hospital, University of Illinois, two days ago and at that time showed a bullous and crusted dermatitis about the ears, mouth, neck, chest, back and extremities. Some of the lesions on the extremities were of multiform type and were grouped. The axillary and inguinal glands were considerably enlarged. The child was abjectly miserable. There were 3,880,000 red blood cells and 16,000 white blood cells per cubic millimeter, with 49 per cent lymphocytes, 2 per cent mononuclear cells, 47 per cent neutrophils and 2 per cent basophils.

DISCUSSION

DR. UDO J. WILE, Ann Aror, Mich.: I think it is difficult in this case to differentiate severe dermatitis herpetiformis from juvenile pemphigus. I prefer the latter diagnosis. A third possibility that would have to be ruled out is that of a bullous iododerma.

DR. HOWARD J. PARKHURST, Toledo, Ohio: I have seen this patient almost from the onset. Following tonsillitis a bullous eruption appeared on the face and extremities, resembling erythema multiforme. The eruption failed to subside, and in view of the grouping of the bullous and vesicular lesions the diagnosis of dermatitis herpetiformis was decided on. There was eosinophilia, and there was also a large number of eosinophils in the contents of the bullae. The cultures made from the vesicles were negative. She was given an arsenical preparation by mouth and intramuscularly and also a course of injections of whole blood intramuscularly. More recently she has been given vitamins, and for a considerable number of months she was exposed to the sun and more recently to artificial ultra-

violet irradiation. Lately insulin has been administered to stimulate her appetite. The eruption has subsided partially at times but never completely, and she has had recurrent showers of lesions at irregular intervals. The mouth has not been involved. At present she seems to have a new flare-up.

DR. UDO J. WILE, Ann Arbor, Mich.: May I venture a simple suggestion, that the child's urine be tested for iodine? There are some patients who are so susceptible to small amounts of iodine that they may break out severely from the iodine contained in iodized salt. The members will surely recall the case recorded by Drs. Eller and Fox (ARCH. DERMAT. & SYPH. **24**:745 [Nov.] 1931) in which a diagnosis of mycosis fungoides was made by some and of various malignant conditions by others and which turned out to be one of fatal nodular iododerma. This patient had not taken iodine in any other amounts than that which is in iodized salt.

DR. CLARK W. FINNERUD: You may recall 2 patients that I showed from the Children's Memorial Hospital years ago. The diagnoses of bullous dermatitis herpetiformis were accepted. In neither child was there evidence of appreciable itching. They differed from this patient today in that both responded to large doses of solution of potassium arsenite U. S. P. In both of them there was anything but classic dermatitis herpetiformis. In 1 patient the lesions were clear bullae; in the other there was a pustular element, but both children were high strung and irritable and in this respect gave a different picture from this child today. However, I am inclined to think that the condition in this case is an unusual bullous dermatitis herpetiformis.

DR. M. OPPENHEIM (by invitation): The clinical features of the child presented by Dr. Senear remind me of impetigo herpetiformis. This disease occurs mainly in pregnant women and in women after parturition. But there are reports of the disease in men too. In these cases of impetigo herpetiformis a calcium deficiency in the blood was found, and disease of the parathyroid glands was suggested. Administration of parathyroid extract improved the condition and cured it sometimes. I suggest trying parathyroid in this case after the determination of calcium in the blood is made.

A Case for Diagnosis (Lupus Vulgaris Erythematodes, Leloir?). Presented by DR. J. R. DRIVER (by invitation), Cleveland.

M. M., a man aged 44, who had lived in Russia (Ukraine) until the age of 17, consulted me first in November 1933, complaining of an eruption on the forehead of three years' duration. The eruption at this time consisted of two discrete, irregularly shaped, reddish indurated papules above the left eyebrow, the surface of which was rough and scaly. There were no apple jelly nodules. Diagnoses of lupus erythematosus, tuberculous verrucosa cutis, Boeck's sarcoid and syphilis were considered. The Wassermann and Kline reactions were negative.

Histologic examination of tissue removed showed a thin epidermis, with plugging of the follicles. In the corium there was edema, with thickened collagen fibers. Especially around the hair follicles and deep in the corium there was a dense cellular infiltrate of mononuclear cells, fibroblasts, plasma cells and eosinophils. There were no giant cells.

One treatment with solid carbon dioxide apparently cleared the process for about two years. In February 1936 another similar treatment was given.

The patient was not seen again until May 21, 1937, at which time the lesions on the forehead were practically gone. However, he now complained of "sore patches" on the roof of his mouth of four or five months' duration. Examination revealed an extensive eruption involving the posterior third of the hard palate, the entire soft palate, the uvula, the tonsils, the pillars and to some extent the walls of the pharynx. The process appeared granulomatous, the mucous membrane was thickened and nodular, and patches of leukoplakia covered most of the surface. Histologic examination of tissue removed from the palate revealed the structure of a granuloma, with infiltration of lymphocytes, fibroblasts and plasma cells. There were no giant cells or tubercle formations.

At this time a course of injections of mapharsen was given, without benefit. Light freezing with solid carbon dioxide and acetone and later cauterization with the actual cautery were of only partial, mostly temporary benefit.

In January 1939 the patient was hospitalized for further study. Roentgenograms of the chest were normal, and cultures on sugar-proof mediums were negative. Tissue from lesions on the face and from the mouth was removed again, and the histologic appearance of the cutaneous lesions was essentially the same as that shown previously. Histologic examination of the tissue from the palate showed a stratified squamous epithelial layer, which was covered by a moderately thick layer of keratohyalin. Beneath the epithelium the tissue was densely infiltrated with great numbers of small round cells which had almost no cytoplasm and dense, round nuclei. There were also a few plasma cells and some larger mononuclear cells which had vesicular nuclei. No giant cells were seen, and there were no areas of caseation or tubercle formation. There was a moderate degree of fibroblastic proliferation, and some new blood vessels were formed. No parasites were seen. The pathologists at Lakeside Hospital interpreted the condition as chronic inflammation of the soft palate.

Inoculations of guinea pigs with material from the oral lesions gave negative results for tuberculosis. Examination of the blood revealed 5,530,000 erythrocytes and 4,500 leukocytes per cubic millimeter, with a differential count of 54 per cent polymorphonuclear leukocytes, 35 per cent lymphocytes, 7 per cent large monocytes and 4 per cent eosinophils. An intradermal test with oidiomycin 1 : 100 (Lederle) gave a positive reaction, with pseudopods. Smears from the palate were negative for tubercle bacilli, yeast, spores and mycelial threads. Serologic tests for syphilis again gave negative results. Physical examination otherwise gave negative results.

Further painting of the oral lesions with a mixture of solid carbon dioxide and acetone produced some improvement. The last treatment was given on July 6, 1939.

A Case for Diagnosis (Lupus Pernio?). Presented by DR. F. E. SENEAR, DR. M. R. CARO and DR. H. C. SCHORR (by invitation).

J. D., a white man aged 50, is presented. Lesions first developed on his cheeks in February 1937. The eruption spread gradually, and by May 1937 the entire face was involved and swollen. The swelling and inflammation persisted all summer but subsided during the following winter. The lesions have persisted since then, with itching and smarting after exposure to the cold and after the ingestion of certain foods, such as eggs, tomatoes, tea and citrous fruits. The lesions are not aggravated by heat or sunshine.

Physical examination shows no abnormalities except those of the skin. Fluoroscopic and roentgenographic examination of the chest showed no evidence of recent or active changes. The urine was normal. The Kahn reaction of the blood was negative. Examination of the blood showed 100 per cent hemoglobin and 6,200,000 erythrocytes and 8,400 leukocytes per cubic millimeter, with a normal differential count.

On each cheek there is a palm-sized, circumscribed, dusky red patch, which extends down to the jaw. Within this there are many pinhead-sized slightly elevated papules. On the chin, root of the nose and top of the nose and forehead there are poorly defined patches of scattered pinhead-sized dusky red soft papules. There are patches with slight dry scaling on the lobes and outer rims of the ears. Diascopic examination shows no apple jelly nodules.

Histologic examination of tissue removed from the lobe of the right ear showed a flattened epidermis, with a moderate amount of intracellular edema. The corium is edematous, with dilated lymphatics and blood vessels. There is a diffuse infiltration of lymphocytes, with fewer histiocytes, and this infiltration is packed more densely about the blood vessels and hair follicles. Acid-fast bacilli were not found with the Ziehl-Neelsen stain.

Lupus Vulgaris. Presented by Dr. David V. Omens and Dr. Walter W. Tobin (by invitation).

A woman aged 47 states that she has had an eruption on her face for approximately thirty years. It began with a small area on the right cheek and slowly enlarged until at the present time the entire face is involved. Also, in the past five years similar eruptions have occurred on the upper part of the arms. The disease resulted in scarring, with deformity about the nose. There has been only occasional itching. Approximately twenty years ago a strong solution was applied to the face which seemed to do harm. Since that time she has had irregular treatments with roentgen rays, but to no avail; in fact, the last series of such treatments, six months ago, seemed to her to make the eruption worse.

She is of Nordic extraction and was born in this country. She is married and has had 4 children, and all members of the family save her are free of this disease. Examination discloses a diffuse involvement of the face and a few scattered coin-sized lesions on the shoulders and arms. The eruption consists of a mixture of erythema, scaling, soft, apple jelly-colored nodules and contractile scarring, which has resulted in the beaklike nose and an ectropion of both eyes. The serologic tests of the blood gave negative results, as well as the examination of the urine. Roentgen ray examination of the chest showed no abnormalities. The tuberculin test with a dilution of 1 : 1,000 gave a negative result, and a biopsy of one of the nodules showed the presence of tubercles with giant, round and epithelioid cells.

DISCUSSION ON PAPERS OF DR. DRIVER, DRS. SENEAR, CARO AND SCHORR AND DRS. OMENS AND TOBIN

Dr. H. E. Michelson, Minneapolis: Dr. Driver's case is interesting to me because the cutaneous lesions look like lupus vulgaris, but the microscopic section did not come up to my expectations. When lupus vulgaris is progressive it is apt to become hypertrophic, and when it is receding it is prone to be atrophic. I think that application of radium to the lesions of the mouth would be the best treatment.

Dr. Carl W. Laymon, Minneapolis: Dr. Michelson and I have been fortunate in seeing a number of patients recently whose lesions resembled those in the patient presented by Drs. Senear, Caro and Schorr. In my opinion, this eruption is a sarcoid. Other eruptions, however, which are clinically similar present a histologic picture which is not consistent with a diagnosis of sarcoid. Some bear more of a clinical likeness to lupus miliaris disseminatus faciei except that the lesions are smaller and more numerous. These have been termed micronodular tuberculids by Pautrier and other French observers, who believe that they are to be closely alined with acnitis except that the lesions do not progress to necrosis clinically and remain tiny nodules. Undoubtedly some cases of such eruptions have been presented under the title of rosacea-like tuberculid, a term which seems to place undue emphasis on the clinical features of another disease entirely unrelated to tuberculosis.

Dr. S. W. Becker: I thought that the microscopic section from the lesion on the forehead in the case of Dr. Driver showed lupus sebaceus and that the lesion in the mouth showed round cell infiltration, with no changes in the epidermis, and suggested lupus erythematosus. I saw nothing clinically or microscopically that would suggest lupus vulgaris.

Dr. Paul A. O'Leary, Rochester, Minn.: When one is obtaining a specimen of skin for biopsy it is advisable to include a piece of normal as well as of pathologic skin. In contrast, when obtaining a specimen of mucous membrane for biopsy, the material should be excised from the center or middle of the pathologic process rather than from the periphery. This is especially true in lesions of the tongue where the surrounding inflammatory reaction is usually intense and might explain the absence of tubercles in the sections from the lesion in Dr. Driver's patient.

Dr. Louis A. Brunsting, Rochester, Minn.: The appearance of the face recalls to my mind 2 patients whom I have observed who presented a diffuse

erythema of the face, with miliary nodules suggesting lupus miliaris follicularis. Microscopic examination, however, revealed evidences of disseminated lupus erythematosus plus deeper foci with the infiltrative structure of sarcoid. This combination is decidedly unusual.

DR. CLARK W. FINNERUD: In regard to Dr. Driver's patient, I expected to find a histologic picture of lupus vulgaris and was surprised to find characteristic changes of lupus erythematosus.

DR. M. OPPENHEIM (by invitation): I believe that one must consider rosacea in Dr. Senear's case. I think the condition is rosacea due to exposure to low temperatures. The symmetric involvement of both ears and the absence of typical scars, without infiltration, suggest to me rosacea with perniosis.

In Dr. Driver's case the clinical diagnosis does not seem to be completely confirmed by the histologic observations. The clinical features are those of lupus vulgaris.

DR. OLIVER S. ORMSBY: My conception of lupus pernio is based on a study of many patients. There are two distinct conditions described under this title. Lupus pernio, described originally by Hutchinson, eventually terminates in lupus erythematosus. In its early stages there is an erythematous eruption on the face, nose and ears that varies in activity for a period and finally becomes permanent and is then typical lupus erythematosus. In the early and more transient stage the lesions resemble chilblain. Lupus pernio of Besnier, which is now considered sarcoid, is a condition in which there is a condition of lesions, erythematous nodules and plaques on the face, fingers, hands and toes. Sometimes they break down and ulcerate, or they may be absorbed, leaving atrophy. On diascopic pressure brown nodules remain. This type is therefore tuberculous, whereas lupus pernio of Hutchinson is lupus erythematosus. I should consider this case of Drs. Senear, Caro and Schorr not as one of rosacea but rather as one of some form of tuberculosis.

DR. H. E. MICHELSON, Minneapolis: I think it is a good rule in dermatology never to diagnose against positive evidence. Since the patient presented by Drs. Senear, Caro and Schorr has polycythemia, it is a bit bold to venture another diagnosis. Had I not known of this condition of the blood, my first thought would have been sarcoid. The microscopic section did not give me any particular lead, and I think that further biopsies of tissue from various areas will have to be performed before it is possible to make a decision.

DR. F. E. SENEAR: It was long after encountering the case that we became aware of the polycythemia that was present.

I agree with Dr. Ormsby that this condition cannot be considered rosacea, even of severe degree, one reason being the distinct evidence of atrophy in the flush areas of the cheek. I felt that there was definite atrophy here. We shall try to follow Dr. Michelson's suggestion and get another specimen for biopsy, because Dr. Caro said that the specimen we had was not taken sufficiently deep to be satisfactory.

Liposarcoma. Presented by DR. FREDERICK R. SCHMIDT.

H. P., a white man aged 50, was first seen on July 25, 1939, suffering from an ulcerated mass on the neck of several months' duration. He did not remember having a lump there previously. The hardness of this tumor suggested actinomycosis, but no actinomyces were found.

Covering the anterior chest wall and the clavicle were 5 hazelnut-sized, elevated, hard, smooth nodes. The Wassermann reaction of the blood was negative. The blood picture was suggestive of leukemia; there were 100,000 leukocytes per cubic millimeter, chiefly mature polymorphonuclear leukocytes.

The patient died three months later, but an autopsy was not performed.

Tissue removed from the mass in the neck and the tumor of the skin histologically showed the presence of large cells scattered singly and in groups through-

cut the section. These large cells contained detritus. Their cytoplasm was granular, and the nuclei were situated in the center and at the periphery. The cells were surrounded by strands of reticulum. The large cells showed fat droplets when stained with sudan III.

Adenoma Sudoriferum. Presented by DR. FREDERICK R. SCHMIDT.

L. J., a white woman aged 69, came to the Grant Hospital in May 1939, with a small tumor of the right hip. This had appeared three years previously and had gradually grown in size to 3 cm. in diameter. It was skin colored, slightly elevated and freely movable in the skin.

Examination of the gross specimen showed that the epidermis was thinner. Filling the entire corium was a more or less sharply circumscribed area composed of cells arranged singly and in groups between fasciculi of connective tissue. These cells, many of which were arranged as alveoli with a central lumen filled with a homogeneous material, were cuboidal, with a small, darkly staining nucleus, resembling in structure those of a mature sweat gland. Differential staining with Masson's trichrome aniline blue and with a nile blue sulfate stain clearly showed the characteristics of a sweat gland.

NEW YORK DERMATOLOGICAL SOCIETY

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Jan. 23, 1940

Eczema Simulating Lymphoblastoma (Mycosis Fungoides). Presented by DR. EUGENE F. TRAUB.

D. S., a man aged 42, is presented from Welfare Hospital, Welfare Island. The patient's father and a cousin suffer from asthma; a sister has hay fever, and a cousin has eczema of the hands. The patient's eruption began in March 1937, one week after an attack of coryza. The first manifestation was itching and dryness of the skin of the right leg and then of the entire body, followed by cracking, scaling, elevated, erythematous patches. The patient was treated with linseed oil, solution of calcium hydroxide U. S. P. and sun baths, and the eruption had cleared up by May 1937. On being tested, he was found to be sensitive to spices. In September 1937, after a coryza, generalized itching developed, and then red papules appeared over the back. The skin cleared up entirely after two weeks in Florida, but when he returned to New York the itching and red plaques recurred. The condition remained in a severe state until September 1938, when it improved briefly with sun baths. Two injections of milk are said to have "caused the skin to break out in all kinds of blotches." "Extraction of infected teeth caused purulent discharge from the legs." Histologic examination at Kings County Hospital in 1938 was reported as showing mycosis fungoides.

Examination shows a thickened lichenified eruption, with generalized plaque-like disks, and scattered individual discrete papules, including lesions on the glans and shaft of the penis.

The patient's maximum and minimum weights have been 182 and 126 pounds (82.6 and 57.2 Kg.), respectively. His present weight is 136 pounds (61.7 Kg.). Urinalysis gave negative results. A blood count showed 4,200,000 erythrocytes per cubic millimeter, 80 per cent hemoglobin and 7,500 leukocytes per cubic millimeter, with 55 per cent polymorphonuclear leukocytes, 43 per cent lymphocytes and 2 per cent monocytes.

Histologic examination showed slight acanthosis. There was an occasional degenerated epithelial cell in the corium. In the upper third of the corium, including the papillary layer, there were small collections of leukocytes arranged in nodules and streamers. Some of these were perivascular. The majority of these cells were lymphocytes and mononuclear leukocytes. There were a moderate number of plasma cells and occasional polymorphonuclear leukocytes and eosinophils. An occasional mitotic figure was noted in these focal collections of cells. There were some connective tissue condensation and slight edema of the papillae. The foci of inflammatory cells were small and not particularly numerous. A diagnosis of chronic inflammatory reaction of the skin was made. The lesions showed several criteria of early lesions of mycosis fungoides.

The treatment during his present hospitalization has been the removal of as many foci of infection as possible, injections of typhoid vaccine, the application of many local ointments and lotions and three treatments with roentgen rays.

DISCUSSION

DR. J. FRANK FRASER: I disagree with the pathologist who made a diagnosis of mycosis fungoides on the basis of the microscopic findings. I also disagree with the clinicians who made that diagnosis. I cannot see any features of mycosis fungoides in the slides which the presenter has exhibited. In regard to the clinical picture, in my opinion there is not a single feature in the gross appearance of the lesions that would lead me to consider the diagnosis of mycosis fungoides. I agree with Dr. Traub that the condition in this case is chronic eczema.

DR. EDWARD R. MALONEY: I agree with Dr. Traub's clinical interpretation in this case.

DR. GEORGE C. ANDREWS (by invitation): The condition looks like eczema of internal origin, and I suggest looking for focal infections, especially in the teeth, and perhaps giving the patient sulfanilamide.

DR. GEORGE MILLER MACKEE: I also am unable to accept the diagnosis of mycosis fungoides on the basis of anything I saw in the patient or under the microscope. Under the microscope there is a perivascular infiltration, for the most part of lymphocytes, with a number of eosinophils. From my rather hasty examination I could see no evidence of granuloma and certainly none of mycosis fungoides. At the same time I think that any eczema that lasts for years and is more or less generalized and even somewhat intermittent must be considered as a possible potential mycosis fungoides. There are many patients who have been treated for eczema for years and occasionally for psoriasis and are finally found to have mycosis fungoides. With this variety of eczema the discoid lesions constitute a prominent feature, and pruritus is severe, but lichenification, allergy and atopy are not so manifest as with neurodermatitis. This variety might be called discoid eczematoid dermatitis.

DR. A. BENSON CANNON: I am convinced of the diagnosis of dermatitis with lichenification due to a sensitization, most likely to some local irritant. I reported 8 such cases at the meeting of the American Dermatological Association in June 1938 (ARCH. DERMAT. & SYPH. **39**:846 [May] 1939), in all of which I found that there was a history of allergy either in the families or in the patients themselves. Several of my patients reacted to pollens and several to drugs. In 3 patients an onset of asthma or urticaria followed by the characteristic dermatitis appeared after the use of a local irritant; in 1 case it was coal tar; in another, clorox, and in a third, pyrethrum. Invariably patients suffering from this type of dermatitis, simulating at times a disease of the lymphoblastoma group, were greatly benefited or cured by a change of climate. I have some 35 patients who have suffered from the disease for years and who have been cured by going to Hot Springs, N. Mex., or to Texas, Arizona, California or Florida. Occasionally such a sufferer will get well by going to a northern climate. It sometimes happens that a patient may have to change to one or more sections of the country before he

becomes free from the condition. I saw 2 patients, who had spent about ten years in hospitals in various parts of the country, become well in a few weeks after arriving at Hot Springs, N. Mex., and they have remained so for three years while engaged in work in El Paso, Texas. I have just had 2 patients suffering with the same type of dermatitis become well within a week to ten days after taking sun and ocean baths in Florida. They broke out with a violent attack of the condition four days after coming back to New York. The patients on reaching a southern climate almost invariably describe a feeling of mental and physical relaxation, freedom from itching and a rapid clearing up of their skin. Regardless of what one's view may be of these varied, distressing symptoms, one cannot avoid the inference that environment plays a vital role in the production of the lesions, and the only cure that I know of is a change of climate, more often to one with warm sunshine.

DR. HOWARD FOX: I agree with the members who do not consider this case to be one of mycosis fungoides. The eruption is generalized, symmetric and profuse, which speaks against this diagnosis. There are also many scratch marks, which are seldom seen in patients with mycosis fungoides. In spite of the fact that the disease causes severe itching, the patient rarely tears the skin with the finger nails. Finally, in my opinion, the individual lesions do not look like those of mycosis fungoides. There is no variation in infiltration in different lesions or in different parts of the same lesion, such as is often present in patients with mycosis fungoides. I agree entirely with what Dr. Cannon said about climate and have advised numerous patients with obstinate generalized eruptions to visit, or if necessary to live in, a warm climate, such as that of Arizona, Florida or southern California.

DR. PAUL E. BECHET: I agree with those who are against the diagnosis of mycosis fungoides. One of the excellent reasons advanced against that diagnosis is the enormous number of lesions present. Mycosis fungoides does not usually present the multiplicity of lesions this patient exhibits. On the other hand, he presents the common picture of generalized itching eczematoid dermatitis, which is seen so frequently in the hospitals.

DR. FRANK C. COMBES: I agree with the diagnosis of chronic discoid and lichenoid dermatosis for the reasons which have been stated, and I do not think this man will get well until he is sent away. He might get some temporary improvement from heat therapy, but I think any improvement will be temporary.

DR. JEROME KINGSBURY: I agree with all the previous speakers that the case is not one of mycosis fungoides. I can imagine, however, that at times some of these lesions may have presented an appearance that would have warranted a consideration, temporarily at least, of that diagnosis.

DR. EUGENE F. TRAUB: I should like to add only one or two points. In the first place, I am delighted that my interpretation, despite the fact that the histologic report from two hospitals was of mycosis fungoides, was accepted by the members. After all, the one thing that would exclude the diagnosis of chronic discoid and lichenoid eczema would be a definite histologic picture of mycosis fungoides. Dr. Fraser's opinion, on examination of the section, that this condition is not mycosis fungoides rules that out. The second point I want to make is that in this type of case there has always been a decided difference of opinion as to whether or not the patient is allergic to something. This patient comes from a family with a definite history of hay fever and asthma, and he has been found to be sensitive to a number of things. That, of course, would not exclude a diagnosis of mycosis fungoides. Dr. Cannon has repeatedly emphasized that point, but it is contrary to the experience of Sulzberger and Garbe (ARCH. DERMAT. & SYPH. **36**:247 [Aug.] 1937). In their 9 cases, they reported no history of allergy in the family, and the patients were not sensitive to cutaneous tests. In some of the cases that have been under my observation I have felt that there was a definite allergy to bacteria or fungi and, in some, an environmental allergy. A point that made me feel that the condition in this case was not mycosis fungoides

was that there were areas of healthy skin between the lesions. Also, this eruption was in no way configurate, with the horseshoe-shaped and eccentric lesions typical of mycosis fungoides. That picture, together with the lesions on the penis, which are unusual in mycosis fungoides, although they could occur, make me feel that clinically the diagnosis of mycosis fungoides can be ruled out.

Recurring Erythema Multiforme Associated with Pregnancy. Presented by DR. JEROME KINGSBURY.

E. C., a woman aged 36, married, has a daughter, now aged 15, by her first husband, and 4 other children, aged 4, 3, 2 and 1 years, by her second husband. She has now been pregnant four months. During all her pregnancies of the past five years the patient has had a generalized pruritic eruption. The eruption began as a rule within the first three months of the pregnancy and did not clear up until after delivery. There is a history of syphilis, with a considerable amount of treatment about fourteen years ago. The Wassermann reaction now is negative, and all tests in recent years are said to have given negative results. The present eruption has been active for the past three months. It is inflammatory and involves the trunk, the neck and the extremities. The lesions are large and elevated, with a tendency to circinate arrangement. There are no vesicles or pigmentation.

DISCUSSION

(The members agreed unanimously with the diagnosis as presented.)

Recurrent Painful Ulcerations of the Lower Lip. Presented by DR. JOSEPH J. ELLER.

N. B., a man aged 52, is presented for Dr. Lloyd H. Kest. Examination eight months ago showed that the lower lip was scaly, fissured and crusted, with pigmented areas. The patient gave a history of having had this condition more or less for two and one-half years. He was under treatment by various physicians. At times there was almost a complete disappearance of the lesions, but at no time were they entirely gone. The ulcerations are painful.

The patient states that he had an appendectomy twenty years ago, followed two years later by an operation for a varicocele. Eight years ago a routine Wassermann test of the blood gave a 4 plus reaction. The patient knew of no sore on the penis or other eruption on the body previous to the present condition. He received continuous treatment for over two years for the positive Wassermann reaction, followed by intermittent treatment for four years. Two Wassermann reactions during the past few years were negative, but an examination two days ago gave the following results: cholesterol antigen, 4 plus; crude antigen, 1 plus; Kline test, 3 plus, and Kline diagnostic test, negative.

On examination today there are no signs of ulceration, crusting or scaliness on either the upper or the lower lip. The lower lip, however, is pigmented in some areas and shows a thinning of the mucous membranes, particularly on areas previously ulcerated.

During the past three years the patient has been treated by different dermatologists and has received roentgenotherapy, local applications of wet dressings and various salves and intravenous injections of gold and sodium thiosulfate and bismuth subsalicylate. The patient has been limited to the use of bland mouth washes, has abstained from drinking alcoholic beverages and smoking, and has not used any irritating lotions or remedies on his face after shaving. Microscopic and cultural examinations for fungi gave negative results. The buccal mucous membranes showed superficial whitish striations resembling somewhat lichen planus.

The following diagnoses were considered: drug eruption (this has been ruled out), dermatitis venenata, allergy, lupus erythematosus, some fungus infection, cheilitis (in connection with light sensitivity) and lichen planus erythematosus.

The patient responded best to applications of a bland emollient such as white petrolatum, and alternating injections of gold sodium thiosulfate, later alternating with a bismuth compound. He was also given vitamin B complex by mouth. Despite satisfactory improvement, there have been recurrences under this treatment.

DISCUSSION

DR. A. BENSON CANNON: I suspect lichen planus. The white, lacy membranes covering the cheeks are characteristic of that condition. The slight, warty thickening in the center opposite the second molars on the right cheek may also be found in cases of lichen planus. The outline of the lip lesion with the raised threadlike border and scaly center may also be lichen planus. The telangiectatic blood vessels in this lesion suggest excessive irradiation.

DR. EUGENE F. TRAUB: Naturally it is difficult to make a positive diagnosis in a case like this on first inspection. It is my opinion that the lesion on the right buccal mucosa, although it certainly looks like lichen planus, is perhaps not the most characteristic part of this eruption; the lesion on the left side of the dorsal surface of the tongue and the one on the lip which extends from the right buccal mucosa in one continuous plaque on to the vermilion border of the lip are the most characteristic. While I have not frequently observed leukoplakia extending out on the vermilion border of the lip, nevertheless I think this diagnosis is more likely than lichen planus or lupus erythematosus. The fact that the patient has had syphilis also seems to favor the diagnosis of leukoplakia.

DR. FRANK C. COMBES: I agree with what Dr. Traub has said about the diagnosis in this case being leukoplakia. There are large, apparently rough plaques on both cheeks, particularly the left one, extending on to the upper lip on the left side. The patches further back along the mucosa are suggestive that this man may bite the oral mucosa there with his teeth. The whole thing looks to me like leukoplakia plus the traumatic lesions.

DR. GEORGE MILLER MACKEE: The patient told me that at times the lip was absolutely normal. If that is so, I do not think the condition can be leukoplakia. Lichen planus and lupus erythematosus must be considered.

DR. JOSEPH J. ELLER: The man at times had definite ulcerations, with bleeding, crusting and extreme pain, so that he was conscious of it all day and even had trouble sleeping at night. The lesions would break down without any trauma. After healing, the lesions would glisten with a thin epithelial layer over the previously ulcerated areas. The condition looks better today than it has in the six months I have had him under treatment. He improved under treatment with alternating intravenous injections of gold and sodium thiosulfate and a bismuth compound. Does any one think the condition might be lupus erythematosus?

DR. EUGENE F. TRAUB: Regardless of the history, the lesions on the tongue seem to me to be leukoplakia without doubt. The ulceration which comes and goes may be, and not infrequently is, a part of leukoplakia.

A Case for Diagnosis (Dermatophytosis of the Keratotic Type?). Presented by DR. HOWARD FOX.

A. F., a bill poster aged 43, was referred from the Veterans Administration Facility. Two years ago an epithelioma was removed from the center of the lower lip. He now presents a dime-sized patch of leukoplakia adjacent to the scar on the vermilion border of the lip.

For the past six years he has had patches of keratosis on the palms and soles. They are sharply defined, greatly thickened, yellowish white verrucous areas. Those on the soles are somewhat tender and cause pain on walking. Many of them have a reddish areola. On the palms the lesions are present on the hypothenar eminences, the largest being 2 inches (5 cm.) in diameter. There is also a small patch on the radial side of the right index finger. The eruption on the sole is more profuse and is present on the bearing surface of the toes, the

balls of the feet, heels and parts of the center of the soles, the patient being rather flat footed. The finger nails are normal, but the toe nails are considerably thickened, opaque and yellowish and show moderate elevation of the distal parts above the nail bed. There is considerable hyperhidrosis of the palms and soles.

The patient previously suffered from Dupuytren's contraction, which was successfully treated by roentgen rays. During this treatment the patches on the hypothenar eminences were also irradiated and disappeared temporarily but recurred at the end of three months. The patient shows patches of typical vitiligo on the backs of the hands.

He states that the paste he uses in his work consists solely of starch and water, and that he usually prepares it himself. He gives no history of arsenical or other medication. Examination of the urine, before and after intravenous injection of sodium thiosulfate, showed no arsenic. The patient states that he has never had gonorrhea. He has no stricture of the urethra; the complement fixation test for gonorrhea gave a negative reaction, and no gonococci were found in the prostatic secretion. He has never had any swelling or pain in the joints. A general physical examination showed no abnormality. A microscopic examination of scrapings from a lesion on the sole showed a small amount of mycelium. The trichophytin test gave a negative reaction.

DISCUSSION

DR. A. BENSON CANNON: I have never seen lesions such as this man presents other than in cases of psoriasis, and had Dr. Fox not told of finding the fungus of ringworm in scrapings taken from the scaly areas, I should have diagnosed the case as psoriasis.

DR. EUGENE F. TRAUB: My impression was that this patient had a rather unusual psoriasis, and I suggest that a biopsy be performed to exclude or confirm that diagnosis. The finding of fungi would not necessarily exclude the diagnosis of psoriasis, because it is possible to find fungi in lesions that are not due solely to ringworm. I recall a patient with tertiary syphilis who presented a squamous eruption on the sole in a configurate pattern suggesting a tertiary lesion, the Wassermann reaction being 4 plus, and fungi were found in the lesion. The fact that the trichophytin reaction was negative would not rule out the diagnosis of a fungous infection, because in a fair percentage of cases, up to 20 per cent, the regular twenty-four to forty-eight hour reading of a trichophytin test may be negative even when fungi have been found or a dermatophytid has been present. This has been recorded by a number of observers. Therefore, it appears that in this case there are two possibilities which have not been ruled out.

DR. GEORGE MILLER MACKEE: My tentative diagnosis would be psoriasis of an unusual type. I agree with Dr. Traub that a negative result of a trichophytin test does not rule out dermatophytosis, but I do not agree that it does not rule out dermatophytid. I doubt if there can be a dermatophytid with a negative trichophytin reaction. I agree with Dr. Traub that a fungus may be a saprophyte.

DR. J. GARDNER HOPKINS: I have never seen hyperkeratoses like these in cases of psoriasis. Whether such lesions can appear at this time of life, I do not know. They are perfectly symmetric, and the horny formations like stalactites hanging off the toes are most striking. One sees pictures of them in cases of Hong Kong foot, which is a fungous infection. The only ones I have seen were in cases of congenital keratoderma or ichthyosis hystrix.

DR. GEORGE MILLER MACKEE: The toe nails are badly involved too. They could be evidence of either psoriasis or onychomycosis.

DR. HOWARD FOX: I should like to know Dr. Cannon's opinion about arsenic as a possible cause of this eruption.

DR. A. BENSON CANNON: I believe that two types of arsenical keratosis are recognized, the more common one consisting of horny plugs on the soles and palms which sometimes undergo epitheliomatous changes. This type of keratosis

is usually found in patients who have been taking solution of potassium arsenite U. S. P. or arsenic trioxide U. S. P., while the other type is the uniform hyperkeratosis of the soles and palms, symptoms seen after ingestion of arsphenamine. Occasionally one may find a combination of the two types of lesions in the same patient. Sometimes one may be aided in the diagnosis of palmar and plantar keratosis due to arsenic by the finding of eczematized areas in other parts of the cutaneous surface or of brown pigmented areas of skin. I believe that the absence of arsenic in one's urine does not necessarily mean that the patient has not a retention of arsenic. One may find large quantities of arsenic in the blood and none in the urine. When arsenic is found in the urine, it is usually thought that the patient is excreting the metal and probably will eventually eliminate the drug from his system.

DR. HOWARD FOX: I felt reasonably sure that both gonorrhea and arsenic could be excluded as causes of the keratoderma in this case. I also felt that the diagnosis of hereditary keratoderma was improbable. The two most likely possibilities seemed to be the keratotic type of fungous infection and psoriasis. The changes in the toe nails could be present in either of these conditions.

Bromoderma with Peculiar Purpuric Lesions. Presented by DR. PAUL E. BECHET.

T. A., a woman aged 32, from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, states that her eruption has been present for eight months and that it appeared several weeks after the administration of elixir of three bromides N. F. for nervousness. Since that time she has taken the drug at intervals. The lesions consist of "shotty" dark red papules and pustules scattered over the face, trunk and extremities. The purpuric lesions are not different from the ordinary simplex variety and can be seen on both the legs and the arms, particularly about the knees and elbows.

DISCUSSION

DR. HOWARD FOX: This picture is not the ordinary one of acne due to bromide, in which the lesions are somewhat tender papulopustules. These are small, flat, indolent papules. However, as the patient has been taking bromides for the past eight months I think a bromoderma should be considered.

DR. GEORGE MILLER MACKEE: I suppose that diagnosis can be accepted tentatively, but it seems to me that the eruption on the legs in addition to being purpuric is also erythematous and could be classified as erythema multiforme or erythema toxicum. Eruptions of that sort can be caused by various drugs, but rarely by bromides, although it is possible for bromides to do it. The possibility of a coincidence must be considered. The condition may be erythema multiforme in a patient who happened to be taking bromides. The acneform lesions do not seem to be numerous enough to make one sure that the condition is due to bromides. The diagnosis of bromoderma is at least doubtful.

DR. EUGENE F. TRAUB: I agree with what has been said, especially about the purpuric lesions. In looking over the literature about bromoderma, I do not recall that purpuric lesions were ever a part of the condition. The patient states that the condition appeared relatively recently on the legs, and as nearly as I could make out, it followed the taking of several tablets of acetylsalicylic acid and some other remedy which her physician had prescribed for a cold. It may, therefore, be a dermatitis medicamentosa but due to some remedy other than the bromide.

DR. FRANK C. COMBES: I doubt that this condition is bromoderma, for the reasons Dr. Fox has stated. The lesions are not nearly inflammatory enough, nor are they tender. I feel that further study and observation are needed in this case before the blame for the eruption can be put entirely on bromides.

DR. PAUL E. BECHET: To my mind the acneform lesions on the face are definitely due to the bromides. They are characteristic. They are rather hard and discrete, with no evidence of seborrhea, comedos or pustules. Therefore, the lesions on the face conform, according to my experience, to the typical acne occurring after prolonged ingestion of either member of the halogen group. As for the question of purpuric lesions in cases of bromoderma, I have never observed a case, but it seems plausible to assume that the two conditions are allied. In 3 cases of iododerma observed some years ago, there were purpuric and even hemorrhagic and gangrenous lesions. Therefore, I do not see why one cannot observe hemorrhagic lesions in cases of bromoderma, and I am under the impression that there are reports of it. The patient gave me a different history from the one given to Dr. Traub. She said the entire eruption occurred a month after she took the bromides.

Epidermolysis Bullosa Acquisita. Presented by DR. PAUL E. BECHET.

L. M., a woman aged 43, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital in December 1939, for relief of a severe bullous eruption of one year's duration. The lesions consist of large vesicles and bullae, particularly numerous on areas exposed to trauma, such as on the hands and legs. The patient states definitely that bullae arise within twenty-four hours after a scratch or a bruise. A large bulla developed on one tibia after she struck it against the bath tub the previous day. The buccal mucosa is affected. On the backs of the hands are numerous milia-like nodules and the scarring which is so characteristic of the disease. A tendency for the lesions to group is not present, and pruritus is not marked.

The Wassermann and Kahn reactions were negative. Histologic examination showed epidermolysis bullosa.

DISCUSSION

DR. J. FRANK FRASER: I disagree with the diagnosis of epidermolysis bullosa on the basis of the microscopic findings. The histologic picture of epidermolysis bullosa is not specific; none of the bullous lesions are. There are some features, the position of the vesicle for example, which may lead one to favor one diagnosis or another, but these are not sufficiently characteristic to make a diagnosis on histologic grounds alone. The diagnosis in the present case must rest on the correlation of the histologic and clinical pictures. In my opinion this correlation is perfect, namely, microscopic vesicles and gross lesions which are typical of dermatitis herpetiformis.

DR. JOSEPH J. ELLER: I agree with Dr. Fraser regarding the diagnosis of dermatitis herpetiformis. I shall therefore not be surprised if this condition eventually develops into pemphigus.

DR. GEORGE C. ANDREWS (by invitation): I believe a drug eruption should be considered strongly, although I admit the likelihood of dermatitis herpetiformis.

DR. GEORGE MILLER MACKEE: I suppose the diagnosis of epidermolysis bullosa was based on two features: histologically, the subepidermic bulla or vesicle, and clinically, the traumatic lesions. In this particular instance, I do not think that these features combined are enough to warrant an unequivocal diagnosis of epidermolysis bullosa acquisita. The intense itching, generalization, grouping and long duration are in favor of Duhring's disease, and I think that in cases of severe, long-standing dermatitis herpetiformis one occasionally sees not only the traumatic feature but even in some instances a Nikolsky sign or pseudo Nikolsky sign and subepidermic vesicles on the hands. At present I am unwilling to rule out dermatitis herpetiformis.

DR. HOWARD FOX: Clinically, I think this case is a classic one of Duhring's disease. The so-called cardinal symptoms are present, including polymorphism, grouping, severe itching and a chronic course with tendency to relapse. This is apparently confirmed by Dr. Fraser's opinion of the microscopic section.

DR. FRANK C. COMBES: I agree with those who made the diagnosis of dermatitis herpetiformis reservedly. The patient is a fairly intelligent woman, and there are certain things in her history that are difficult to overlook. One has been already mentioned, the development of a bulla within fifteen minutes of trauma. Also, she awakes in the morning with bullae on her elbows from friction of the sheets when she turns over in bed during the night. I have never heard of that occurring in cases of dermatitis herpetiformis. I should like to know the cell count of the contents of the vesicles and whether eosinophilia is present. The potassium iodide test might be of some aid in differentiating between dermatitis herpetiformis and epidermolysis bullosa.

DR. PAUL E. BECHET: I admit that the lesions resemble dermatitis herpetiformis. On the other hand, as was just pointed out, there is no doubt that trauma produces these lesions. They are most prominent on the ankles, legs and hands, places usually exposed to trauma. She presents numerous milia-like small nodules on the backs of her hands and large scars, both characteristic of epidermolysis. I am still of the opinion that the clinical evidence favors the diagnosis of epidermolysis rather than dermatitis herpetiformis.

Lupus Vulgaris of the Nose. Multiple Pigmented Hemorrhagic Sarcoma. Presented by DR. JOSEPH J. ELLER.

M. C., an Italian aged 82, is presented from the New York City Hospital clinic for Dr. Lloyd H. Kest. The patient has had an eruption confined to the nose and adjacent areas for many years. The eruption has been persistent but has not spread and is erythematous and scaly and shows atrophy. Apple jelly nodules are seen on diascopic pressure.

On the lower portions of both legs and on both feet there are variously sized indurated nodules and plaques of brownish to purplish black. Edema has never been intense. The patient does not understand English, and it is most difficult to elicit a history.

The case is presented to show the presence of lupus vulgaris and Kaposi's sarcoma in the same person. The diagnoses were corroborated by microscopic study.

DISCUSSION

(The members agreed unanimously with the diagnosis as presented.)

Early Atypical Lupus Erythematosus. Presented by DR. PAUL E. BECHET.

H. W., a Negro aged 27, presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, states that his eruption has been present for six months. The patient had a penile chancre eight years previously and received continuous treatment for two years at the Social Hygiene Clinic of the Department of Health. The last injection was given a few days ago. The patient has typical sycosis, but on the right cheek are two erythematous, partially ringed lesions, with a raised but soft border. On the middle of the forehead at the hair line a similar lesion is present. The lesions are approximately 5 mm. in diameter and are not scaly.

Histologic examination showed the early stage of lupus erythematosus.

Hypertrophic Lupus Erythematosus. Presented by DR. PAUL E. BECHET.

F. S., a man aged 49, presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, was previously presented by Dr. Max Scheer before the Manhattan Dermatological Society on Jan. 9, 1940. He says his eruption has been present two and one-half years. The lesions consist of three oval areas, more or less confluent, situated on or about the lower lip and involving most of that area. They are dull red, with hard, raised, indurated,

rolled borders. The central portions are atrophic and scaly. The vermilion border is involved.

Histologic examination confirmed the clinical diagnosis of lupus erythematosus.

DISCUSSION ON DR. BECHET'S CASES

DR. J. GARDNER HOPKINS: The Negro is known to have syphilis, the lesions having a faint raised ridge at the border and a flattened scaly center. I cannot see why those lesions could not be a circinate syphilid or a fixed drug eruption. There seem to be plenty of reasons why they are not lupus erythematosus. There are no infiltration, adherent scales or telangiectases. In the second case I also raise a question about that area with the soft, raised, red ridge at the border. Of course, if it was proved histologically to be lupus erythematosus, one must discard the possibility of sarcoid, but clinically it looks more like sarcoid than like lupus erythematosus.

DR. EUGENE F. TRAUB: In view of what Dr. Hopkins has said, I might say that one of the things in favor of the diagnosis of lupus erythematosus clinically in the case of the Negro is the fact that he has alopecia where the lesions are on the right cheek. In addition to this loss of hair there are erythema and scaling. It would be difficult to conceive of any disease other than lupus erythematosus that would cause loss of hair with erythema and scaling in that location.

DR. HOWARD FOX: I agree with the diagnosis of Dr. Bechet and the remarks of Dr. Traub. I do not agree that this lesion is an annular papular syphilid. This manifestation of syphilis appears during the first six or eight months after infection and usually forms complete circles with hyperpigmented centers. The infection in this case occurred eight years ago, and the patient has had continuous antisyphilitic treatment.

DR. A. BENSON CANNON: I agree with Dr. Hopkins. The Negro's lesions on the forehead and right cheek are suggestive of erythema multiforme due to the arsphenamine that he has had or to phenolphthalein. The lesion on the right cheek is only a macular blush, without infiltration, scaling, atrophy or telangiectasia. Only the lesion on the right side of his forehead is a bit raised at the border, while the others are brownish blue, pigmented, macular and free of scaling. I also agree that the lesion on the skin of the lower lip in the second case is more suggestive of sarcoid than of lupus erythematosus. Again, the location is unusual for lupus erythematosus, and the oval, elevated, blue, shiny, red borders, with the center of the lesion hard and sievelike, are not symptoms that I would expect to find in a case of lupus erythematosus.

DR. HOWARD FOX: In answer to Dr. Cannon's suggestion that this condition might be a phenolphthalein eruption, it should be noted that this eruption has a raised border, which is not present in lesions due to phenolphthalein.

DR. PAUL E. BECHET: Both conditions are indicated histologically, but the clinical evidence is also in favor of the diagnosis of lupus erythematosus. While the Negro has definitely had syphilis, he has had continuous antisyphilitic treatment for two years, the last treatment dating back only a few days ago. The patches show a solid elevated plateau-like ringed lesion, entirely unlike the usual annular syphiloderm so frequently seen in Negroes. The patches have been present for only six months. Early lupus erythematosus is never scaly or hyperkeratotic. Patulous follicular openings, so common in the chronic stage are also absent. As in this case, the early stages of lupus erythematosus become manifest first as erythematous patches of a more or less fixed character, which later undergo edematous infiltration, with raised edges, and it is not until after several months or even years that it assumes the characteristic picture of the chronic discoid type.

The second patient presents the hypertrophic mutilating type of lupus erythematosus, with lesions with greatly indurated, inflamed borders. The condition is fortunately uncommon, as it is particularly resistant to treatment and on healing

leaves most unsightly scars. I have observed cases in which it has eaten away a large section of tissue from the nose and after healing has left a deep punched-out scar.

A Case for Diagnosis (Parapsoriasis? Purpura Annularis Telangiectodes?). Presented by DR. PAUL E. BECHET.

T. G., a man aged 48, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, complaining of an eruption which has been present for seven or eight years. In the summer it practically disappears but always recurs in the winter. As it undergoes involution it leaves dark brown stains. The lesions occur on the abdomen and flanks, as well as on the legs. They are definitely telangiectatic and exhibit a tendency to annular formation.

Two biopsies were performed, one of tissue from an early lesion on the left leg and the other of tissue from a much older lesion. The histologic report suggested parapsoriasis and definitely ruled out purpura annularis telangiectodes (Majocchi's disease).

DISCUSSION

DR. GEORGE MILLER MACKEE: Dr. Bechet said that purpura annularis telangiectodes had been definitely ruled out. I presume this was because of the histologic architecture. I examined the slide, though hastily, and it is true that I did not see any of the characteristic features of purpura annularis telangiectodes. There was no panarteritis, no hyaline degeneration of the arterial walls and no sacculation or herniation of the vessels. These features are all absent, but this may be because only early lesions were examined. In very early lesions there are edema of the blood vessels, perivascular infiltration, edema of collagen and hemorrhage. These features are present in this case. If another biopsy specimen is obtained, part of an old lesion should be selected. I must admit, however, that typical changes usually occur in fairly young lesions. In a typical case there are remissions and exacerbations, but the exacerbations may persist for three, six or even eight months or possibly a year. Sooner or later, though, there is a remission, which may also last for months. I understand that this patient is free from active lesions during the summer. The large size of the lesions does not speak against purpura annularis telangiectodes. There is such a thing as purpura simplex annularis, but usually it does not last for months. I think there is at least a fair possibility that this case is one of aberrant purpura annularis telangiectodes. Most patients have arthritic pain, but not all of them.

DR. EUGENE F. TRAUB: Dr. MacKee said something about generalized lesions. This patient has something rather indefinite on the left side of the trunk, but so far as I can tell, the eruption is limited to the lower extremities, from the hips downward.

DR. GEORGE MILLER MACKEE: There are four lesions on the arms.

DR. EUGENE F. TRAUB: I do not think that dermatitis hemostatica is found on the upper extremities, but otherwise I do not see how one could exclude that diagnosis in a case of an eruption on the legs which comes and goes as this one does.

DR. HOWARD FOX: My conception and that of the average dermatologist about purpura annularis telangiectodes is rather hazy. I should like to ask Dr. MacKee, who has made a special study of this disease, whether he knows of any case of eight years' duration in which the eruption has cleared up every summer.

DR. PAUL E. BECHET: There are lesions on the abdomen and the flanks as well as on the extremities. This case is most interesting but difficult to discuss, in view of the histologic report by Dr. Sachs that the microscopic examination was definitely against purpura annularis telangiectodes and in favor of parapsoriasis.

Arsenical Keratoses. Presented by Dr. A. Benson Cannon.

L. B., a girl aged 10 years, was presented before this society on Dec. 19, 1939 (Arch. Dermat. & Syph. **41**:962 [May] 1940), with a diagnosis of arsenical keratoses of the palms and soles.

Examination showed a high amount of arsenic in the blood, 0.25 mg. per hundred grams of dried blood. Her physician reports that he has established the fact that the thickening of the palms and soles appeared after treatment of her congenital syphilis with neoarsphenamine. He also states that the soles and palms cleared up after administration of arsphenamine was stopped, but the condition reappeared after resumption of the neoarsphenamine, and a generalized exfoliative dermatitis appeared. The child's palms and soles have improved rapidly under treatment directed toward the elimination of the arsenic.

Leukemia and Leukemid. Presented by Dr. Eugene F. Traub.

E. D., a woman aged 64, was presented before this society on Dec. 19, 1939 (Arch. Dermat. & Syph. **41**:964 [May] 1940). At that meeting it was recommended that a biopsy be performed of one of the lesions on the fingers. Unfortunately, before I saw her again, she had received a ¼ skin unit dose of roentgen rays (75 r) on these lesions, and all of them had disappeared. When I saw her a few days ago, practically all of the cutaneous lesions, with one or two exceptions, were gone. Lately bullous lesions have been developing, which are quickly ruptured and become covered with a thick crust. None of these lesions have seemed suitable for biopsy, but should one develop that appears to be a leukemid, I shall try to obtain a biopsy specimen. The itching and other subjective symptoms are much improved.

BRONX DERMATOLOGICAL SOCIETY

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Jan. 25, 1940

Poikiloderma Vasculare Atrophicans (Jacobi). Presented by Dr. Paul Gross.

J. R., a man aged 39, has had a generalized eruption for the past three years, which began after an intensive exposure to sunlight. He has received various topical applications and injections but was never treated with roentgen rays. His general condition is good. He complains of dryness of the skin and a burning sensation in the cutaneous lesions.

The extensive eruption involves the trunk, arms and thighs and is made up of two types of lesions. The more recent lesions are yellowish pink, oval plaques, the size of half a dollar and covered with fine dry scales. The more advanced lesions are the size of a palm and larger, are dark red or cyanotic and consist of telangiectasia, mottled pigmentation and depigmentation. There are slight erythema and moderate scaling in these patches. The skin of the larger plaques shows wrinkling.

The Kahn and Kline reactions were negative. Urinalysis showed no abnormalities. Examination of the blood showed a normal value for hemoglobin and a normal cell count. Histologic examination of an early lesion showed normal epidermis, with slight hyperkeratosis in several places and a slight perivascular infiltration, with small round and occasional polymorphonuclear cells. Examination of an advanced lesion showed the epidermis to be of normal thickness, but the rete pegs were wiped out in several areas, and there was a definite invasion of the deeper layers by inflammatory cells. The corium showed a rather massive infiltration, with small round cells, few polymorphonuclear and eosinophilic leuko-

cytes and larger cells with pale nuclei. There were also some phagocytes containing brown pigment. In the subpapillary layer there was perivascular infiltration. The capillaries were somewhat increased in number but were of small caliber.

Poikilodermatomyositis. Presented by DR. PAUL GROSS.

A. B., a woman aged 30, born in Puerto Rico, was presented before the New York Academy of Medicine, Section of Dermatology and Syphilis, in November 1939 (ARCH. DERMAT. & SYPH. **41**:1187 [June] 1940).

Since that presentation there has developed on the right thumb an irregular yellowish area the size of a lentil and surrounded by a bluish zone of erythema. The yellowish infiltrate is firm and tender and suggests a deposit of calcium in the skin. There is also a contracture of the flexor tendons of the left palm.

DISCUSSION ON CASES OF DR. GROSS

DR. WILBERT SACHS: The histologic structure in both cases is interesting. In the case of poikiloderma vasculare atrophicans the upper part of the cutis shows a rather dense cellular infiltrate, which is composed almost entirely of small round cells. The elastic tissue in the upper part of the cutis is either fragmented or absent. The absence of polymorphous cellular infiltrate, reticulum, mitotic figures and Poutrier abscesses rules out mycosis fungoides. The simple inflammatory process, the telangiectasia and the loss of the elastic tissue are characteristic of poikiloderma vasculare atrophicans.

In the case of poikilodermatomyositis the changes throughout the upper part of the cutis are similar to those in the first case. However, while the inflammatory process is somewhat less pronounced, the elastic tissue is entirely missing. In the lower portion of the section the muscle fibers are thin and closely packed. They are all arranged in rows, lying parallel with the epidermis. The elastic tissue in this area is fragmented. The changes in the upper portion are not unlike those found in poikiloderma vasculare atrophicans. In the deep portion, however, there are absorption and atrophy of muscle.

DR. LOUIS CHARGIN: Dr. Sachs pointed out, as have certain other authors, that poikiloderma and dermatomyositis differ histologically as well as clinically. The case presented as one of poikiloderma is typical. The case of poikilodermatomyositis is questionable. It is true that now and then dermatomyositis in its later stages may present changes in the skin that are not clinically unlike that of poikiloderma, but certainly not early in the course of the disease. Neither in course nor in histologic picture are they identical; they are two entirely different diseases. Poikiloderma is an inflammatory disease, and dermatomyositis is a degenerative disease.

DR. HENRY SILVER: I also am of the opinion that little is gained by classifying the two diseases as one. I regard poikiloderma as a condition which is classified primarily with the cutaneous atrophies, and Dr. Sachs just pointed out that until one finds changes in the elastic tissue one should not make the diagnosis of poikiloderma. Secondary involvement of various organs has been recorded by Petges and Cléjat, Jacobi and others. In other words, poikiloderma Jacobi is a condition which originates in the skin and is characterized by reticulated markings, thinning and wrinkling, pigmented spots, telangiectases, capillary hemorrhages, follicular brown-red pinpoint-sized and larger papules, red and bluish discolorations and whitish atrophic areas. Dermatomyositis, on the other hand, must be regarded as a systemic disease involving the skin, muscles and nervous system to a varying degree.

DR. PAUL GROSS: In the second case the diagnosis of poikilodermatomyositis is well established. The first case I consider of special diagnostic interest, because the histologic section of the advanced lesion of poikiloderma showed such massive infiltration that mycosis fungoides could well be considered. I was glad to hear from Dr. Sachs that he is able to rule out mycosis fungoides on histologic grounds.

The main purpose of presenting these cases together was to show the distinction between poikiloderma Jacobi and poikilodermatomyositis. It is true that the cutaneous changes in dermatomyositis differ considerably from those in poikiloderma and that there exists a resemblance to lupus erythematosus of the acute variety. The scleroderma-like changes are the end product of the process in the skin, just as the sclerosis of the muscle is an end product of the myositis. Yet I do not agree with Dr. Chargin that the condition is primarily a degenerative process. The inflammatory reaction of the skin and muscle during the earlier period of involvement is too pronounced, and the vascular damage in both tissues has been referred to recently by Guy, Grauer and Jacob (ARCH. DERMAT. & SYPH. **40**:867 [Dec.] 1939).

Bismuth Line in the Long Bones of a Newborn Infant. Presented by DR. SAMUEL FELDMAN.

This 1 month old infant is the child of Mrs. M. L., aged 30, who was presented before this society in October 1939 (ARCH. DERMAT. & SYPH. **41**:765 [April] 1940), with a lichen-planus-like eruption following the taking of arsphenamine.

The infant was apparently normal on physical examination. The Wassermann reaction of blood from the umbilical cord was negative. Roentgenograms of the bones revealed the presence of a heavy metal shadow (bismuth) manifested as a transverse line near the end of the diaphysis, particularly in both femoral and tibial bones and less marked in the ulnar and radial bones.

DISCUSSION

DR. LOUIS CHARGIN: According to Caffey (*Am. J. Dis. Child.* **53**:56 [Jan.] 1937), there is a definite relation between the time when bismuth is administered to the pregnant woman and the position of the bismuth line in the long bones, as judged by the roentgenogram. The position of the bismuth is directly related to the period of pregnancy, and the width of the line is determined by the amount of metal given. In the animal, Caffey has shown by experiment that the important anatomic change is the replacement of calcified cartilege matrix for the bone marrow spaces.

DR. FRANK E. CROSS: In a prenatal syphilis clinic of the department of health routine roentgenologic studies of the long bones of infants were made about two weeks after birth. Some of the children had bismuth deposits in the epiphyses of the long bones.

DR. SAMUEL FELDMAN: The roentgenologist expressed the view that the line is comparable with any lead, arsenic or gold line, which is occasionally seen in the long bones of adults who have been given these metals. Since the mother did not come in contact with any of these metals, and since the administration of arsenic to the mother was discontinued after the second injection and treatment was continued with a bismuth compound only, it follows that this case is one of bismuth absorption and deposit in the bones. In the light of Dr. Chargin's remarks about the time when the bismuth line appears, it would seem that the condition is in an early stage. There is also a definite deposit of new bone over the bismuth line.

Eczema Venenatum Due to Wooden Bracelet. Presented by DR. MARION B. SULZBERGER.

S. T., a woman aged 52, was admitted to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Dec. 31, 1938, with a sharply defined vesicular eruption on the left forearm above the wrist. Under routine local therapy the patient showed decided improvement during the second week of treatment and did not return to the clinic.

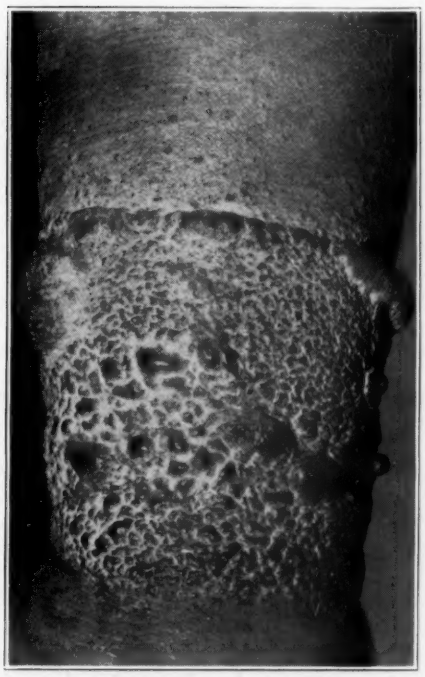

Fig. 1.—Four day old bullous reaction on the arm after the wearing of a wooden bracelet for only two hours.

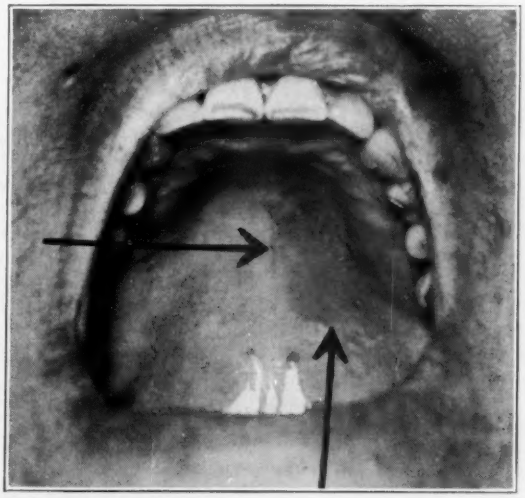

Fig. 2.—Reaction of mucous membrane of palate to scrapings of wooden bracelet.

On Dec. 19, 1939 the patient was readmitted, with a vesiculobullous erythematous eruption about 2 to 3 inches (5 to 7.5 cm.) wide encircling the right forearm just above the wrist.

Questioning disclosed that on December 16 the patient had worn a wooden bracelet for about three hours, which caused intense pruritus and some erythema. Several hours after the removal of the bracelet the eruption appeared. The same bracelet had been worn on the left forearm for several days about one year ago. The dermatitis last year was apparently due to the same cause.

On Dec. 19, 1939 the mucous membrane of the left side of the hard palate was tested by applying scrapings from the wooden bracelet and holding these in place for five minutes. An erythematous papular lesion appeared at the site within forty-eight hours and disappeared within five days.

The family and personal history were not significant. There was no history of asthma, hay fever, urticaria or infantile eczema.

DISCUSSION

DR. FRANK E. CROSS: When Dr. Sulzberger performs patch tests on this woman he will probably find that the dermatitis is due to the shellac or varnish covering the wood. I should like to mention the case of a young boy who presented a dermatitis under the chin. The chin rest of the violin was suspected. Patch tests with the varnish coating were performed, and a severe bullous reaction resulted in four hours. Judging from the severe dermatitis present in this case I should expect a similar reaction from the patch tests.

DR. CHARLES LERNER: I think that the eruption can be caused by the wood itself and not necessarily by the shellac. A short time ago I had a case of cheilitis in a musician, caused by French reed used in the mouthpiece of the musical instrument he played. The condition cleared entirely when Italian reed was substituted. Neither strip of wood had been covered with shellac.

DR. MARION B. SULZBERGER: I was unable to complete the tests to see what ingredients of the wood caused the dermatitis. The patient was presented because of the high degree of sensitivity and to show the severity of the local reaction as well as the associated sensitivity of the mucous membrane. As Dr. Shelmire has recently shown, this association of mucosal sensitivity with cutaneous sensitivity in allergic eczema venenatum is more common than was previously supposed.

Eczema Venenatum from Nail Polish. Presented by DR. MARION B. SULZBERGER.

R. C., a woman aged 37, was first seen at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Nov. 14, 1939. The family history disclosed no cases of asthma, hay fever or cutaneous eruptions. The patient had been well until November 1938, when an itching eruption began on the eyelids and lips. The eruption gradually extended and eventually involved practically the whole face and neck, as well as the arms and chest. The patient received elsewhere a variety of treatments which consisted of roentgen rays, injections of sodium thiosulfate, estrogens, vitamins in high doses, ultraviolet and infra-red irradiation and fever therapy. The treatment was without effect. The eruption improved somewhat when she remained at home and did not use any cosmetics.

The patient presents redness and scaliness of both eyelids and a scaly, erythematous, scratched and somewhat thickened skin on the sides of the face and neck, on the chest and in the cubital spaces. The appearance of the eruption suggested a contact dermatitis, possibly due to some cosmetic. Patch tests performed with various cosmetics gave negative results. Attention was then called to the fact that nail polish and nail polish foundation had been omitted, and these were tested. The reaction to nail polish was 3 plus and to nail polish foundation 1 plus. On

closer questioning, it was then found that the onset of the dermatosis had occurred shortly after the first use of a new type of foundation for the polish.

With the use of soothing local treatment and the discontinuation of application of the nail polish and foundation, the patient improved rapidly and within a few days was entirely free of the eruption. She remained entirely well until patch tests with the offending preparations were performed, on December 26. Within twenty-four hours after this application, the previously affected areas showed a recurrence of the original dermatitis.

DISCUSSION

DR. MARION B. SULZBERGER: The patient is presented to call attention once more to this form of dermatitis. It occurs in women who are sensitive to one or more ingredients of the polishes used on their finger nails. The favorite sites are the eyelids and the face and not the hands or periungual areas. One has therefore to bear that in mind and to consider finger nail polish in investigating the eczematous eruptions of the eyelids so frequently seen in women.

Generalized Granuloma Annulare. Presented by DR. CHARLES PINES.

D. W., a school boy aged 9 years, was seen at the clinic of Bellevue Hospital on Nov. 23, 1939. The eruption began about eight months ago on the left leg and ankle. In the course of a few months numerous new lesions appeared on various parts of the body. The mother states that some of the lesions have undergone spontaneous involution, while others have remained stationary and have persisted to date. Physical examination gave essentially negative results except for showing enlarged tonsils and postnasal discharge.

On the chest, abdomen and buttocks and both upper and lower extremities there are raised, round or oval lesions with sharply elevated borders. The lesions are of firm consistency, either pinkish or skin colored, with a definite tendency toward grouping, and many have clear centers. There are no subjective symptoms.

The tuberculin test with dilutions up to 1 : 10,000 gave negative results. Scrapings for fungi proved negative.

DISCUSSION

DR. WILBERT SACHS: I agree with the diagnosis of granuloma annulare, but I should like to have histologic confirmation if possible. This may not show granular degeneration. If so, it would be difficult to differentiate between the annular type of sarcoid and this type of granuloma annulare.

DR. H. VICTOR MENDELSOHN (by invitation): I saw this patient previously and hesitated to accept the diagnosis of granuloma annulare because of the multiplicity of the lesions and the limited number of typical lesions and because there was little or no tendency to spontaneous involution. However, the cases recorded in the literature, especially the one presented by Dr. Wise in which there were lesions on one hand and follicular lesions on the feet (ARCH. DERMAT. & SYPH. **40**:291 [Aug.] 1939), bear great resemblance to the case presented. The histologic examination proved all the cases to be of granuloma annulare. I believe that this case is also one of granuloma annulare.

DR. DAVID BLOOM: Generalized eruptions of granuloma annulare are rare. I presented a little girl with such a condition (ARCH. DERMAT. & SYPH. **37**:905 [May] 1938), who had less infiltrated lesions. While the lesions on the elbow do not suggest granuloma annulare, the diagnosis can be definitely made from the lesions on the body.

DR. HENRY SILVER: Is the generalized type of granuloma annulare more frequently observed in adults or in children? The few patients that I have seen were adults.

DR. CHARLES PINES: I believe that this condition is more frequently observed in children.

Chronic Discoid and Lichenoid Exudative Dermatosis. Presented by Dr. Marion B. Sulzberger.

A man aged 34, born in Poland, gives no family history of asthma, hay fever or cutaneous diseases. With the exception of undergoing an operation in 1932 for an inguinal hernia he was in good health until 1937, when the present eruption appeared on the thighs. The eruption cleared soon but recurred six months later. The patient was treated without success at Beth Moses Hospital, at the Essex Street Dispensary and at the King's County Hospital. In the last institution the eruption cleared in about six weeks but again recurred in two weeks, in August 1938. Ambulatory treatment until December was of little benefit. The patient was subsequently admitted to Montefiore Hospital for Chronic Diseases, where he remained until October 1939. The eruption cleared completely but relapsed within two weeks after he was discharged from the hospital. In December he was readmitted to the hospital.

The face, extremities and trunk present papular and discoid eruption. The lesions are round or oval and coalesce, forming bizarre shapes. There are numerous excoriations. The lymph glands are enlarged.

Examination of the blood showed 4,780,000 erythrocytes and 13,750 leukocytes per cubic millimeter, with 27 per cent eosinophils, 54 per cent neutrophils, 1 per cent basophils, 8 per cent small lymphocytes, 6 per cent large lymphocytes and 4 per cent lymphoblasts. Examination of bone marrow, according to the method of Arinkin, revealed an increase in eosinophilic polymorphonuclear leukocytes and the presence of eosinophilic myelocytes. A smear from the bone marrow showed 6 per cent myelocytes, 2 per cent myeloblasts, 2 per cent primitive cells, 10 per cent normoblasts, 11 per cent lymphocytes, 3 per cent monocytes, 48 per cent segmented polymorphonuclear leukocytes, 6 per cent staff cells and 12 per cent eosinophils. Histologic examination of an axillary lymph node showed subacute nonspecific lymphadenitis. The chemical examination of the blood showed 95 mg. of sugar, 8.2 mg. of urea, 150 mg. of cholesterol, 9.8 mg. calcium, 3.5 mg. of phosphorus, 4.4 mg. of albumin, 3.2 mg. of globulin, 0.3 mg. of bilirubin and approximately 0.02 mg. of lead per hundred cubic centimeters and no arsenic. The Wassermann reaction with a cholesterol antigen was negative. The Kahn reaction was negative.

DISCUSSION

Dr. Charles A. Greenhouse: Have any mental symptoms been observed in these patients, particularly during the periods of recurrence? It has been my experience that during an acute exacerbation there were definite symptoms of psychosis accompanied by moderate rise in temperature and superficial pustulation.

Dr. Leo Spiegel: I believe that all the patients whose cases were described by Sulzberger and Garbe were males. Have any cases been observed in which the condition occurred in females?

Dr. Marion B. Sulzberger: I have observed no definite example of this dermatosis in the female with the exception of a questionable one in a middle-aged woman. I have observed about 35 cases of this disease. I do not think there is anything noteworthy about the psyche of the patients excepting that itching, lack of sleep and other distressing effects of this chronic recurrent and incapacitating disease would cause the patient to act somewhat psychotic. However, other possibilities still exist, namely, that the nervous system may also be involved or may become involved as a result of the cutaneous disease.

Dr. Eugene F. Kelley: Concerning the psychosis factor, I can report a case in which the patient was sensitive to turpentine and had repeated attacks of dermatitis from contact with it in his occupation. During the last attack he became comatose. All the symptoms cleared immediately after a spinal tap; the fluid was under pressure. The neuropsychiatrist was of the opinion that the meningeal irritation was probably due to sensitivity to turpentine.

DR. ADOLPH ROSTENBERG: I have observed a number of these cases. Of course, the patients suffered a great deal, but they were not neurotic. I do not think there is a neurogenic factor in these cases.

DR. MARION B. SULZBERGER: One sees a fairly typical picture in most cases, and the disease is easily diagnosed. It is about twelve years since I first began to observe these cases. I was first struck by the peculiarity of this dermatosis in Zurich and became more and more impressed by the fact that I could not fit it into any known group of dermatoses. It is important to stress that in none of my cases has the condition gone on to true lymphoblastoma (Sulzberger, M. B., and Garbe, W.: ARCH. DERMAT. & SYPH. **36**:247 [Aug.] 1937). On the contrary, the patients with the older conditions have all become free of lesions, are well and are going about their work. If this disease were a forerunner of mycosis fungoides or lymphoblastoma, one would encounter more cases of lymphoblastoma, because the dermatosis is a relatively common condition. Then, too, the dermatosis is seen entirely in men, and lymphoblastoma has no sex predilection.

Serpiginous Syphilid and Nonsyphilitic Aortitis. Presented by DR. ARTHUR SAYER.

L. W., a laborer aged 63, born in Germany, has been living in the United States since 1893. He came to the clinic of Mount Sinai Hospital in December 1939, on account of vertigo, weakness and a cutaneous eruption of a few months' duration.

The patient presents a symmetric diffuse papular eruption on the upper and lower extremities. The lesions have the color of raw ham, are discrete and the size of a pea or grouped in serpiginous patches 2 to 3 inches (5 to 7.5 cm.) in diameter. There is moderate generalized adenopathy. The patient states that this cutaneous eruption has been present for the past five months. The Wassermann reaction was 4 plus.

He gave a vague history of a penile sore about forty years ago. He was never treated for syphilis. The blood was tested years ago, and the Wassermann reaction was found to be negative. He did not recall having had a recent penile lesion before the onset of the eruption.

The neurologic examination gave essentially negative results except that the left pupil was found to be slightly larger than the right. The urinalysis showed normal findings. The systolic blood pressure was 105 and the diastolic, 70. Electrocardiogram tracings showed the QRS complex to be blurred and the T wave in lead III inverted, changes indicating cardiac involvement. A roentgenogram of the chest showed no abnormalities in the lungs, the heart slightly enlarged and the aorta diffusely dilated and tortuous, most marked in the ascending portion and the upper part of the descending portion.

DISCUSSION

DR. LEO SPIEGEL: The lesions on the wrist impressed me as late serpiginous syphilid. I cannot offer a diagnosis for the lesions on the shoulder; clinically they are follicular papules. With regard to the aortitis, what evidence can Dr. Sayer furnish that it is not based on syphilis? Judging by the history which the patient gave, namely, that he had had a penile lesion forty years ago for which he was treated with "rubs," it appears that the aortitis is due to syphilis.

DR. LOUIS CHARGIN: The lesions on the hands especially suggest serpiginous papular syphiloderm and are likely a form of late secondary syphilis. The eruption is bilateral. Bilateral syphilitic eruptions are rare with late syphilis, but they do occur. Concerning the question of the nonsyphilitic character of the aortitis, I think the burden of proof is on the presenter. Certainly in a man of this age who had an infection many years ago and now presents a dilated aorta, the aortitis is more likely to be on a syphilitic basis.

DR. ARTHUR SAYER: There is no doubt in my mind that the man has a serpiginous syphilis and that the infection is rather recent. The history of a penile

lesion forty years ago is too vague to be accepted and certainly should not be considered as a primary lesion on that evidence alone. It could have been a herpes progenitalis or another type of nonsyphilitic lesion. The reason I believe the aortitis is nonsyphilitic is that his recognized syphilis is comparatively recent and could not cause this type of visceral lesion so early. Furthermore, the roentgenologist reports that the location of the aortitis and its tortuous character are against its being of syphilitic nature. It is also to be remembered that strenuous labor is occasionally responsible for aortitis—or, as Osler said, "Vulcan as well as Venus may cause aortitis."

Keratosis Follicularis (Darier). Presented by Dr. Harry B. Feiler.

L. G., a woman aged 21, was first seen about three months ago. She states that the lesions on the face, chest and thighs appeared about two years ago. No other member of the family is similarly affected. The father has psoriasis.

On the lateral aspect of the face, extending downward to the neck, the lateral and frontal part of the chest and merging at the lower half of the sternum there are grayish brown pigmented areas consisting of keratotic and verrucous lesions, varying in size from that of a pinhead to that of a lentil seed. Similar lesions, but at times so light that they are almost inconspicuous, are observed in the interscapular region and on the inner aspect of the thighs.

Histologic examination showed normal skin in the center of which there was a small lesion. It consisted of an area of hyperkeratosis and was apparently near a follicle or around a follicle. There was a characteristic horny plug containing some incompletely keratinized epithelial cells. There were also some partially degenerated epithelial cells which could be identified as corps ronds. The underlying epithelium showed some cellular irregularities and numerous mitotic figures, particularly in the remaining basal layer. A slight cellular infiltrate was present around the blood vessels in the cutis.

The histologic diagnosis was reported as dyskeratosis, consistent with the diagnosis of Darier's disease.

DISCUSSION

Dr. Marion B. Sulzberger: In spite of the fact that there are so few changes visible in this case, there already are two typical palmar "warts," which one sees so often in cases of Darier's disease.

Dr. Henry Silver: Conditions of this type are known as formes frustes of Darier's disease. It is important to stress that no other members of the family are affected. A few years ago I presented 4 members in one family who had the disease (Arch. Dermat. & Syph. **31**:919 [June] 1935).

A Case for Diagnosis (Early Raynaud's Syndrome?). Presented by Dr. Maurice Umansky.

R. R., a woman aged 23, noted three years ago that the right index finger became white when exposed to cold. She has never experienced any pain or swelling. Recently all her fingers and toes became similarly involved. Blanching occurred even in the summer during spells of chilly weather. Two sisters are afflicted in the same way.

When exposed to outdoor winter atmosphere the hands and feet become cold, clammy and bluish, with a diffuse cyanotic hue. The three middle fingers and toes are dead white, but their tips and the underlying parts of the nails are cyanotic. The radial pulse is the same on both sides. The skin presents no other abnormalities.

The patient gives a history of vague pains of the muscles of the back, shoulder, chest and feet since childhood. She is suffering from chronic left maxillary sinusitis with a postnasal drip and had until eight months ago frequent nosebleeds. Roentgen examination of the cervical portion of the spine showed the presence of spondylitis involving the bodies of the fourth, fifth and sixth vertebrae.

Examination of the blood showed 85 per cent hemoglobin and 8,500 leukocytes per cubic millimeter, with 54 per cent segmented polymorphonuclear leukocytes, 3 per cent staff cells, 39 per cent lymphocytes, 1 per cent eosinophils and 3 per cent monocytes. The sedimentation rate was four hours. The Kahn reaction was negative. The basal metabolic rate was —9 per cent. The urinalysis showed no abnormalities.

DISCUSSION

DR. DAVID BLOOM: This is an instructive case showing the difference between Raynaud's disease and sclerodactylia. With the former the skin is unchanged. Sclerodactylia may be associated with Raynaud's syndrome, for both are manifestations of a disturbance of the vegetative nervous system.

DR. MAURICE UMANSKY: The girl's condition is of a progressive nature. For two years only the right index finger was affected. Since the beginning of this winter all the fingers and toes have become involved. W. A. Pusey (ARCH. DERMAT. & SYPH. **19**:467 [March] 1929) reported the case of a chauffeur who suffered from ischemia of one finger on exposure to cold. He considered the fact that the condition was limited to one finger as rare in the literature. In the light of the case presented the involvement of one finger seems to be an early stage of the condition which eventually spreads to the rest of the fingers. The condition in this case is apparently not due to endocrine disturbance. It is, rather, familial, since other members of the family suffer similarly. The early diagnosis of such a case of Raynaud's syndrome is important from the standpoint of therapy. Sympathectomy has to be considered. In the later stages of the syndrome, when bullae and gangrene set in (the other name of this condition is symmetric gangrene), the treatment is no longer effective.

Pigmentation of the Tongue Due to Bismuth. Presented by DR. CHARLES PINES.

C. C., a Negro fireman aged 38, has been under treatment at the Central Social Hygiene Clinic of the Department of Health for the past one and one-half years for neurosyphilis. On his visit to the clinic on Dec. 12, 1939 he complained of a sore on the tongue of a few days' duration. Examination revealed on the under surface of the right side of the tongue at the margin a tender and painful superficial ulceration covered with a grayish exudate. The tongue showed a grayish coating. The lesion was thought to be either traumatic or due to bismuth. A smear showed a few Vincent organisms. Several days later a bluish black pigmentation was noted on the under surface of the tongue at the site of the original lesion; this has persisted to date. The patch of pigmentation is surrounded by speckled areas of discoloration the size of pinpoints.

DISCUSSION

DR. DAVID BLOOM: I agree with the diagnosis of bismuth pigmentation of the tongue. It is a rare condition, although this case is the third that I have encountered in the past two months. In the other 2 cases which I have observed the pigmentation was located on the dorsum of the tongue. I have always thought that the pigmentation was due to a deposit of bismuth, but I have been recently advised by Dr. Satenstein that the pigmentation is due to melanin and not to bismuth.

DR. FRANK E. CROSS: Usually the pigmentation occurs on the under surface of the tongue. The usual bismuth line does not occur in this location.

DR. LEO SPIEGEL: This is an unusual case of bismuth discoloration in that the deposit is most pronounced in the area where the trauma occurred on the side of the tongue. The patient also has a severe bismuth stomatitis.

DR. CHARLES PINES: I believe that the reason for the development of the bismuth pigmentation on the tongue was largely the local injury sustained.

I recently observed a similar case at the Bellevue Clinic. A woman presented a bluish black line on the gums and discoloration at the tip of the tongue. The patient stated that she frequently pressed the tip of the tongue against the teeth. All who observed the case agreed that this habit, essentially trauma, was most likely the underlying factor in determining the location of the pigmentation.

Eczema Venenatum Due to Lipstick and Nail Polish. Presented by DR. HARRY B. FEILER.

I. V., a girl aged 17, was first seen at the clinic of the Lebanon Hospital in August 1939. She states that in the latter part of June an eruption appeared on the face. When seen in August the patient presented an erythematous, scaly erupion around the right eye, in an area of adjacent skin extending laterally to the hair margin and oblong patches on the right side of the neck. Under soothing local applications the eruption disappeared. One month later there developed a dermatitis involving the lips. An eruption similar to the previous one recurred and again involved the face, neck and ears.

Patch tests with petrolatum, yellow wax, cetyl alcohol, paraffin, stearoricinol (a combination of stearic acid and castor oil), tetrabromofluorescein, brilliant red, royal scarlet, maroon Almay, 0.5 per cent eosin in 80 per cent alcohol, nickel, silver, rouge, oil of bergamot, Marvelous mascara, powder and rouge, mirro-glo nail polish and Beverly nail polish gave negative reactions. Patch tests with Almay perfume, Style-set lipstick and Platinum nail polish gave positive reactions.

DISCUSSION

DR. MARIÓN B. SULZBERGER: It is possible that this patient is sensitive to some essential oil which is present in all three articles to which she gave positive reactions.

In regard to so-called nonallergic cosmetics, they are nonallergic in that there are several important allergens eliminated (orris root and oil of bergamot), but they still contain perfume, dyes, certain essential oils and various other ingredients. A sensitized patient may therefore react to a "nonallergic" cosmetic as well as to any other brand.

PHILADELPHIA DERMATOLOGICAL SOCIETY

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Feb. 23, 1940

A Flesh-Colored Paste to Camouflage Cutaneous Lesions. Presented by DR. JOSEPH V. KLAUDER and DR. ELMER R. GROSS, Wilmington, Del.

Two patients with lupus erythematosus are presented to demonstrate that a paste has made their lesions considerably less apparent, with consequent improvement in appearance, making it possible for 1 of the patients to resume work. The formula of the paste, modified from that of E. Daubresse-Morelle (*Rev. franç. de dermat. et de vénéréol.* **14**:355, 1938), is as follows:

Glycerin	16.3 parts	Titanium oxide	40.0 parts
Distilled water	19.8 parts	Zinc oxide	17.0 parts
Egg albumin	1.0 part	Iron oxide	5.0 parts
Purified siliceous earth	0.1 part	Liquid petrolatum	0.5 part

(Powdered ochre [q. s.] may be added to make a darker shade.)

One patient prefers this application to the proprietary "covermark," since the latter dried and cracked on the skin. Theatrical grease paint was tried but was

discontinued, since it was greasy, rubbed off, did not absorb perspiration and was difficult to remove. None of these objections apply to the paste now being used.

DISCUSSION

DR. FRED D. WEIDMAN: Is there any difference in the satisfactoriness of the application in summer and in winter?

DR. JOSEPH V. KLAUDER: One can easily add a preservative to eliminate the possibility of bacterial action in summer.

DR. FRED D. WEIDMAN: In the laboratory my associates and I use a mounting solution—Farrant's solution—which contains egg albumin, and in order to prevent decomposition we add arsenic. For other watery solutions we use thymol. Arsenic would not be altogether satisfactory as an ingredient of a face cream, but thymol might be satisfactory. In a mixture containing albumin it is necessary to inhibit the growth of micro-organisms.

DR. JOSEPH V. KLAUDER: The odor of thymol might be objectionable in a face cream.

Nonspecific Effect of Antisyphilitic Treatment in Inflammatory Ocular Lesions (Chorioretinitis). Presented by DR. JOSEPH V. KLAUDER.

I. C., a white woman aged 32, was first seen on June 8, 1939, with central chorioretinitis of both eyes. Her complaint was poor vision, which had first appeared three years previously. She had been hospitalized and studied by various ophthalmologists and ineffectually treated by many procedures, including intravenous injections of typhoid vaccines and injections of old tuberculin and streptococcus vaccine. No evidence of a focus of infection could be discovered. Repeated examination of the blood yielded negative Wassermann reactions, and examination of the spinal fluid also gave negative results. Physical examination for syphilis gave negative results, and the family history did not reveal any syphilis. The patient had never been pregnant. Ophthalmoscopic examination of the right eye disclosed opacities of the vitreous; the disk was oyster gray; the margins were blurred, and the macular region was inflamed, with areas of exudative retinal atrophy pigmentation. A clear view of the fundus of the left eye could not be obtained, on account of opacities in the vitreous; the disk was pale, and areas of pigmentation could be seen around the disk. Vision was 1/45 in the right eye and 6/22 in the left. Although the diagnosis of syphilis could not be established, antisyphilitic treatment was administered on June 17. This consisted of 30 grains (1.94 Gm.) of potassium iodide orally three times a day, two injections of an oil-soluble bismuth compound at weekly intervals and neoarsphenamine weekly, beginning with 0.1 Gm. and increasing to 0.3 Gm. Soon after treatment was instituted an appreciable improvement was apparent. The vitreous opacities became less, and the retinal choroidal inflammation began to subside. On June 29 the vision in the right eye was 2/45 and in the left was 6/12. The improvement was progressive, so that in September 1939 examination of the right eye disclosed considerably less opacity in the vitreous; the disk was somewhat whitish; the margins were much less blurred; there was some retinal atrophy about the disk, and in the macular area there was fine, disklike choroidal pigment. The left eye showed less opacity in the vitreous; the disk was blurred, with some swelling of the nasal portion, and about and below the disk there were patches of retinochoroiditis, a blotch of pigmentation and areas of retinal atrophy. In December 1939 binocular vision was 6/9.

Nonspecific Effect of Antisyphilitic Treatment of Patients with Inflammatory Ocular Lesions (Chorioretinitis). Presented by DR. JOSEPH V. KLAUDER.

P. M., a white woman aged 24, was referred to me in September 1939 for testing the nonspecific effect of antisyphilitic treatment of chorioretinitis of the

right eye of four months' duration. Extraction of two teeth, tonsillectomy and treatment directed at a possible sinus infection had no effect on the ocular condition. There was no other clue as to the cause of the chorioretinitis. Repeated Wassermann tests gave negative reactions. The patient is married and has a healthy child aged 3 years. She has had no miscarriages or stillbirths. Her husband stated that he has never had a venereal disease. Physical examination gave essentially negative results. Ophthalmoscopic examination of the right eye showed opacities in the vitreous, and the disk was oval and slightly blurred. Extending from the disk to the temporal side of the retina there were large areas of recent and old chorioretinitis. The vision of the right eye was 4/6. The left eye was uninvolved and had normal vision. Weekly injections of an oil-soluble bismuth compound were started on September 30. These were followed by a course of weekly injections of 0.45 Gm. of neoarsphenamine. Potassium iodide was given orally. Soon after this treatment there was appreciable subsidence of the inflammation. The improvement continued. Two months later there were no active inflammatory areas, and the chorioretinitis had retrogressed.

DISCUSSION OF DR. KLAUDER'S CASES

DR. JOSEPH V. KLAUDER: These cases raise the question as to whether the patient had syphilis, since the regression of the lesions under antisyphilitic treatment was like the response of syphilitic lesions. There was an appreciable improvement, with lessening of the inflammatory reaction, after one injection. However, there was no clinical evidence to support the diagnosis of syphilitic chorioretinitis. I thought it would be worth while to determine the nonspecific effect of syphilitic treatment in patients with inflammatory ocular lesions. The frequent use of mercury by the ophthalmologist apparently exerts a nonspecific effect. I do not know of any series of cases in which the effect of a bismuth compound or neoarsphenamine rather than of mercury was studied. Gold sodium thiosulfate has been used in the treatment of lesions suspected of being tuberculids, but the ophthalmologists are not yet making use of arsenic and a bismuth compound for the nonspecific effect which I believe the substances exert on certain inflammatory ocular lesions.

Old Blood Vessel Remains of Interstitial Keratitis. Presented by DR. JOSEPH V. KLAUDER.

L. C., a white girl aged 16, had active interstitial keratitis in the right eye in 1934, for which she received sixty-seven injections of bismuth subsalicylate and twenty-five injections of neoarsphenamine. The Wassermann reaction of the blood is now negative. There are no stigmas of congenital syphilis. The corneas are clear on gross inspection. However, there are old blood vessels in the right cornea which are diagnostic of interstitial keratitis. These can be demonstrated by slit lamp examination and with the plus 20 lens of an ophthalmoscope.

DISCUSSION

DR. JOSEPH V. KLAUDER: This patient illustrates the importance of the slit lamp in the clinical diagnosis of congenital syphilis. Aside from the history of "sore eyes" and the slit lamp findings, she has no evidence by which the diagnosis of congenital syphilis (interstitial keratitis) could be made.

DR. DONALD M. PILLSBURY: When do you think a patient with interstitial keratitis should be treated with nonspecific therapy? What are the criteria for changing from standard treatment to some form of fever therapy?

DR. JOSEPH V. KLAUDER: I think it desirable to use fever therapy routinely, if only in the form of vaccine in conjunction with standard therapy. My routine is to give a vaccine intravenously every other day in conjunction with antisyphilitic therapy. Malarial therapy is employed in selected cases. If nonspecific therapy is not used routinely, I should select patients in whom the interstitial keratitis is severe or is not progressing favorably.

DR. ALFRED COWAN (by invitation): The slit lamp picture sometimes seen in patients with syphilitic interstitial keratitis is classic. One usually sees a density in the posterior portions of the cornea (a sort of thin, translucent loss of opacity), while the anterior portion of the cornea is clear. The blood vessels may be so small and thin that they may be mistaken for anything but blood vessels. In nearly every case massage of the eye stimulates the circulation sufficiently to make it certain that the structure seen is a blood vessel. In my experience these vessels are permanent, in spite of repeated statements to the contrary. They appear in a peculiar fashion. First one sees endothelial strands, which gradually enlarge to fair-sized vessels. When the acute process subsides, they contain no blood unless they are stimulated by massage. In some cases the interstitial keratitis heals so well that one cannot tell by superficial examination whether the eyes were ever affected. One should never, however, give a prognosis with regard to the end result of interstitial keratitis. I have observed some cases in which the condition was so severe that the corneas were almost as opaque as a piece of paper and yet at the end of about a year the patient had almost normal vision. On the other hand, I have seen apparently mild involvement result in such scarring that the vision becomes seriously affected. I think interstitial keratitis would disappear if one did not give antisyphilitic treatment at all.

Blood Vessels in Cornea Thirty-Five Years After Interstitial Keratitis. Presented by DR. JOSEPH V. KLAUDER.

K. W., a white woman aged 45, when 10 years of age had interstitial keratitis. Treatment consisted only of mercury rubs. She has been married for sixteen years. Her 2 children, aged 15 and 12 years, are in good health, presenting no evidence of syphilis of the third generation. On examination the patient has a suggestive facies of congenital syphilis. Her upper teeth have been removed. There is a small, faint opacity in each cornea. Old blood vessels of interstitial keratitis were seen with the plus 20 lens of the ophthalmoscope, and slit lamp examination of the cornea revealed changes characteristic of old interstitial keratitis (*J. A. M. A.* **113**:1624 [Oct. 28] 1939). The vision in the right eye was 6/30, and with correction, 6/15 plus 1. In the left eye it was 6/21, and with correction, 6/9. The Wassermann reaction of the blood was doubtful.

DISCUSSION

DR. JOSEPH V. KLAUDER: Carvill and Derby (*Boston M. & S. J.* **193**:403, 1925) published a comprehensive study of interstitial keratitis, in which they compared the final vision of treated patients with that of a similar number of untreated patients. In the treated patients the final vision was better.

Interstitial Keratitis at the Age of Sixty. Presented by DR. ELMER R. GROSS, Wilmington, Del.

F. L., a white man aged 60, had bilateral interstitial keratitis at the age of 25, for which he received only local treatment. One young brother had interstitial keratitis. The patient had no recurrence until November 1939, when the right eye became actively involved. Examination reveals that he is edentulous and has a congenital syphilitic facies. He has eighth nerve deafness. The vision in the right eye is 1/60; in the left eye it is 2/60. Slit lamp examination of the right eye showed extensive scarring of all the layers of the cornea, more pronounced in the pupillary and nasal half. There was definite increased relucency of the posterior surface and moderate pigmentation of the scars, especially at the lower third. There was moderate deep vascularization. The anterior chamber was deep. There was slight atrophy of the iris stroma. The lens appeared hazy by reason of the corneal opacities. The left eye showed the same changes as the right eye except that scarring was less extensive. There was definite increase in relucency of the posterior surface, with several deep vessels seen. The lens appeared to be clear,

with increased relucency of the suture lines. The slit lamp diagnosis was old interstitial keratitis of both eyes. The Wassermann reaction of the blood was strongly positive.

DISCUSSION

DR. JOSEPH V. KLAUDER: I think the oldest patient with interstitial keratitis reported in the literature was 70; the youngest was 2 years.

DR. ROBERT KIERLAND (by invitation), Rochester, Minn.: I do not believe that at the Mayo Clinic progress is made beyond what is done here in the management of interstitial keratitis. Nonspecific therapy is used at the clinic, particularly malaria.

DR. JOSEPH V. KLAUDER: How young are the patients you treat with malaria?

DR. ROBERT KIERLAND (by invitation), Rochester, Minn.: The youngest I have seen treated with malaria was 12 years. That treatment is given to any patient over 4 years of age, provided the general condition is good, with careful watching for reactions.

Atrophy of the Optic Nerve. Old Interstitial Keratitis (Malaria Therapy). Presented by DR. MARJORY HARDY (by invitation), Norristown, Pa.

E. B., a white woman aged 21, had "sore eyes" six years ago, for which she received only local treatment. She now complains of almost continuous headaches. Examination reveals a definite congenital syphilitic facies, a high palatal arch, poor dental hygiene, a suggestion of bowing of the right tibia and exaggerated reflexes. Examination of the fundus revealed a pale right disk, with sharply defined edges. The vessels were macular; the periphery was normal. The entire fundus was distorted. The left eye was the same as the right except that pallor of the disk was less evident and was more confined to the temporal side. The pupils were equal and fixed to light. A corneal haze was seen grossly. On Feb. 8, 1939 the vision was 6/60 in the right eye and 6/30 in the left eye. The slit lamp examination revealed old interstitial keratitis of both eyes. Starting on November 13 the patient was given malarial treatments. She had nine major crises. This was followed by the administration of bismuth compound and of neoarsphenamine. The serologic reactions on November 3 were: Wassermann, positive, and Meinicke, weakly positive. On November 10 the examination of the spinal fluid showed: reaction for globulin, weakly positive; colloidal gold curve, 0000000000, and Meinicke reaction, negative. On November 30 the spinal fluid showed: reaction for globulin, negative; colloidal gold curve, 0000000000, and Kolmer reaction, moderately positive.

DISCUSSION

DR. JOSEPH V. KLAUDER: This is the first combination of atrophy of the optic nerve and interstitial keratitis I have seen in this clinic. I have seen patients with interstitial keratitis who have had pupillary abnormalities with normal spinal fluids. The association of active neurosyphilis with interstitial keratitis is not common.

Pemphigus of the Mucous Membranes; Ocular Pemphigus (Remissive Stage). Presented by DR. JOSEPH V. KLAUDER.

M. G., a white woman aged 57, who was presented at previous meetings of this society (ARCH. DERMAT. & SYPH. **27**:718 [April] 1933; **37**:364 [Feb.]; 687 [April] 1938), has been under observation since 1931. She also has argyria and lupus erythematosus of the scalp. During the active stage of the condition lesions were noted in the various mucosal surfaces. A vesicle was seen on the conjunctiva along with acute conjunctivitis; vesicles and erosive areas were present in the mouth; erosive areas occurred on the nasal septum, in the vagina and on the anal mucosa. The oral lesions first appeared in 1920, and the ocular involvement began in 1929. Treatment with injections of gold sodium thiosulfate

and a bismuth compound for the lupus erythematosus seems to have influenced the pemphigus favorably, since it has remained quiescent for a longer period than any time since its appearance. There have been no oral vesicles since about September 1938, and there are only occasionally a few erosive areas. The ocular involvement is now quiescent. The cul-de-sacs are narrowed. The conjunctiva is thickened and wrinkled, and there is an external symblepharon in the right eye. The corneas are uninvolved, and therefore her vision is good. The underlying pathologic process, which causes shriveling of all mucous surfaces, is fortunately concentrated in the mouth and vagina and not in the eye. The vagina is almost obliterated. The patient is shown especially to demonstrate areas of scarring on the buccal mucosa. There is a linear, cordlike scar on the right side. There is a rounded scarred area on the left side of the nasal septum.

DISCUSSION

DR. HOWARD EARLE TWINING: Has this patient ever shown any cutaneous lesions?

DR. JOSEPH V. KLAUDER: No, I observed vesicles only on mucous surfaces. Your patient with ocular pemphigus who was to be presented at this meeting was the only patient I had seen with ocular pemphigus and also bullous lesions on the skin. After reviewing the literature and after studying a number of patients with the disease, I have changed my opinion and now believe that ocular pemphigus is a part of pemphigus of the mucous membranes and is in some way related to pemphigus of the skin.

DR. DONALD M. PILLSBURY: I should like to suggest that in any cases of argyria recorded in the future an attempt be made to determine as exactly as possible how much and in what concentration the silver salt was used. I think these data should be obtained, in view of the new requirements of the Food and Drug Administration.

DR. ABRAM STRAUSS: Why does one rarely see ocular lesions in cases of true pemphigus? Is it because they are distinctive conditions or different clinical aspects of the same condition?

DR. JOSEPH V. KLAUDER: I do not know. There are cases of ocular pemphigus reported in which pemphigus vulgaris subsequently developed with death as the result. The concept of ocular pemphigus embraces the appearance of vesicles on the conjunctiva and usually other mucous surfaces, a subconjunctival inflammation which leads to contraction, shriveling of the conjunctiva and its obliteration. The disease is progressive and is often confused with trachoma. Duke Elder stated that if the patient lives long enough blindness will eventually ensue.

Interstitial Keratitis (Malaria Therapy). Presented by DR. JOSEPH V. KLAUDER.

N. B., a white girl aged 19, when first seen, in November 1939, had active interstitial keratitis of the left eye of one month's duration. The right eye was uninvolved. The left cornea was diffusely hazy. Vision was: left eye, counting fingers at 6 inches (15 cm.), and right eye, 6/6. Slit lamp examination of the left cornea confirmed the clinical diagnosis of interstitial keratitis. The patient had nine attacks of fever, with temperatures ranging from 103 F. to 105 F., beginning on November 16. Prior to malarial inoculation, she received three injections of a water-soluble bismuth compound and three injections of neoarsphenamine. During malaria therapy there was a prompt subsidence of subjective symptoms, and the cornea became less hazy. Administration of the bismuth compound and neoarsphenamine were resumed after the malarial treatments were stopped. Vision in the left eye is now 6/15 plus 1; there is no inflammation, and the cornea shows a faint opacity in the center. The right eye became involved about February 15.

DISCUSSION

DR. JOSEPH V. KLAUDER: It is of interest to note that, although the first eye did well after malarial therapy, the involvement of the second eye was not prevented. An analysis of records of patients receiving different forms of treatment now being conducted although not yet completed shows so far that best results are obtained from fever therapy, in addition to administration of arsenic and bismuth compounds.

A Case for Diagnosis (Dermatitis Herpetiformis? "Id"?). Presented by DR. LEWIS M. JOHNSON (by invitation) for DR. CARROLL S. WRIGHT.

B. R., a white man aged 30, with a history of susceptibility to "sun poisoning" and of having received treatment for "allergic rhinitis," when first seen, on Sept. 29, 1939, presented the typical picture of tinea of the soles and eczematization of the penis and scrotum. The rest of the eruption was suggestive of a dermatophytid. He now presents a generalized dermatitis that occurs in patches, some of which are flat and scaly and others thickened with eczematization and a tendency to crust. These patches tend to coalesce in some areas. He also exhibits considerable excoriation, but the scratch marks are not the predominant factor, since he also shows secondary changes due to superimposed infection. The eruption began in August 1939, as a pruritic vesicular penile eruption. It spread to the groin as a patchy, weeping and crusting papulovesicular dermatitis. Two weeks later it occurred on the hands and feet, and in another week it was on his face and back. This eruption improved somewhat during the occasions when the patient was hospitalized but promptly recurred when he went home, and at present the eruption is practically generalized and extremely pruritic. The patient is well nourished, intelligent and apparently free from any nervous instability. No foci of infection have been detected, but he has a more or less pronounced lymphadenitis. His physical status is normal. The urine is normal. Blood counts on two occasions showed some reduction in hemoglobin, with a normal erythrocyte count. The lymphocytes were somewhat increased, and there were 32 and 21 per cent eosinophils. A serologic test for syphilis gave a negative result. The patient has been given various local applications, chiefly antipruritic and antiseptic, which gave only temporary benefit. He has also had, parenterally, calcium gluconate, vaccines, whole milk and liver extract. Internally he has had alkalinizing medication, massive doses of vitamin D, iodides and sedatives. Mild roentgen ray therapy has improved certain areas only. Histologic study of the skin revealed a possible hematogenous process, such as may occur with rheumatic dermatoses. The picture was inconsistent with that of atopic dermatitis, particularly since the changes occurred so deeply in the tissue. The changes in the lymph node were inflammatory, but the possibility of a lymphoblastomatous process could not be excluded, especially Hodgkin's disease, in view of the eosinophilia.

DISCUSSION

DR. FRED D. WEIDMAN: I have studied the sections from this case. There is at least one miliary abscess deep in the corium, which is hard to reconcile with any of the clinical features seen tonight; and after seeing the dermatosis, I shall have to consider the abscess as being possibly the result of secondary infection. I did find at one place, where there was the least scratching (the posterior axillary fold), a certain annular arrangement of some of the papules. I suggest that this condition may be a beginning dermatitis herpetiformis and recommend the iodide test. The lesions are entirely too sharply circumscribed and discrete for the eruption to be an expression of an atopic dermatitis.

DR. ABRAM STRAUSS: This case is somewhat similar, I believe, to one I presented two meetings ago. The patient was a young Negro from the Eastern Penitentiary, and I believe the consensus then was that he had more or less an "id" eruption.

DR. LEWIS M. JOHNSON (by invitation): I considered the possibility of dermatitis herpetiformis. My first impression was that this condition was an "id," and the lesions on the feet and hands particularly looked as if they might be of fungous origin. However, since then the eruption on the feet and hands has cleared up.

Telangiectatic Dysplasia of the Rendu-Osler-Weber Type, with Pigmentary Changes. Presented by DR. JOSEPH V. KLAUDER.

Mrs. D. T., a white woman aged 50, has had "red spots" on her skin as long as she can remember. Her sister has similar but smaller numbers of "red spots" on her skin, and her mother had the same. The patient does not know whether her sister and mother ever had nosebleed or other hemorrhages. She is subject to nosebleed, having usually two severe attacks each year. The gums bleed easily when she uses a toothbrush. There is no history of other hemorrhages. About twenty years ago a large area of pigmentation appeared on the inner surface of the right arm and subsequently disappeared. Five years ago pigmentation appeared and has since persisted in the axillas, on the upper inner surface of the thighs and on the lower aspects of the legs. She perspires freely; her face flushes readily; she has frequent attacks of palpitation, and she sneezes eight to ten times consecutively some mornings. Her blood pressure is 180 systolic and 85 diastolic. On the flush areas of the face and on the nose there are telangiectatic vessels, with a few red puncta. The lips and buccal mucosa are normal. The tongue is of the scrotal type but is otherwise normal. There are telangiectases on the soft palate and on the uvula. The conjunctivas are normal, and the fundi show no abnormalities of the vessels. On the nasal septum there is a bright red punctum covered with a hemorrhagic crust and with radiating telangiectases. On both surfaces of the upper extremities and on the trunk there are scattered "ruby spots" (De Morgan spots), so-called angiomas. These are bright red, discrete and slightly elevated. On the upper extremities there are a great number of bright red puncta. Pressure around the arms with the cuff of the sphygmomanometer does not increase the number of puncta. On the inner surface of the right arm there are light brown puncta and telangiectasia-like lesions; some are crescentic, and there are two ill defined circinate lesions. Here the appearance is suggestive of angioma serpiginosum. In both axillas and on the upper surfaces of the arms there are discrete spots and irregularly shaped patches of pigmentation, varying from light to dark brown to black. The upper inner surface of both thighs is similarly involved. The pigmentation is more pronounced here, and in the center of some of the pigmented patches there is a bright red spot. On the cubital spaces and on the flexor surfaces of both wrists there are linear and rounded areas of light brown pigmentation. The hands are uninvolved. On the upper part of the chest there are scattered areas of telangiectasia. On the legs and thighs there are scattered bluish arborescent telangiectases of the type commonly seen in women. On the lower third of both legs there are large dilated venules and irregularly shaped areas of reddish brown pigmentation, on the borders of some of which there are pinpoint-sized reddish puncta and telangiectasia-like reddish brown lesions. Here the appearance is suggestive of Schamberg's disease.

DISCUSSION

DR. FRED D. WEIDMAN: William Egbert Robertson (*Ann. M. Hist.* **6**:255 [May] 1934) stated the belief that he had observed the bright lesions appearing during attacks of acute cardiac decompensation. Their location in dependent positions around the ankles and legs of this patient suggests the desirability of studying her circulatory system. The fact that they have been present as long as the patient can remember would tend to discredit the idea that they are the kind of telangiectases about which Dr. Robertson has written. I suppose that the combination of the hereditary vascular weakness with possible cardiac decompensation at this woman's age could explain the localization of the lesions to the dependent position, where factors of stress and strain are in operation.

DR. DONALD M. PILLSBURY: One cannot yet be entirely certain that the pigmentary changes are associated with hemorrhage. In the first place, this woman has a definite stasis, and it seems to me that the lesions on the ankles are compatible with the result of a stasis pigmentation. The axillary lesions did not show definite telangiectases, but the woman is certain that these come and go. They first appeared about twenty-one years ago. The lesions always appear during the summer months, a time when one would expect an intertriginous effect in the axillas. I think a little more proving will have to be done before this case can be accepted as one of Rendu-Osler-Weber syndrome associated with pigmentation.

DR. FRED D. WEIDMAN: I assumed that it had been proved that the condition was Osler's syndrome, in view of the history of epistaxis.

DR. JOSEPH V. KLAUDER: Dr. Weidman's remarks concerning Robertson's explanation of these angiomas is one view. Another view, that of Weber, is that the angiomas are evidence of a telangiectatic dysplasia. That view would exclude capillary weakness as a cause. It is true that the pigmentary changes might not be part of that condition, but I believe they are. The patient obviously has a pathologic process involving the capillaries. The picture she presents is not a typical Osler's syndrome. Telangiectases in the Osler syndrome are most common on the hands, lips and tongue, but this patient has none at these sites. She does not have any of the spider type of telangiectases, which are also frequently seen with Osler's disease. On the thigh she has pronounced pigmentary patches, and in the centers of some of them are definite angiomatous red puncta. I think it is reasonable to associate the pigmentation with the capillary condition. I believe this patient's condition belongs in the group of diseases reported by Weber as telangiectatic dysplasia of the Rendu-Osler type (*Brit. J. Dermat.* **51**:468, 1939).

NOTE.—The patient states that she did not use cologne water or any cosmetic in the axillas or on the upper inner surfaces of the thighs. Her sister has a number of angiomas and red puncta scattered over the surfaces of the arms and legs, with fewer on the skin of the trunk; she is not subject to nosebleed.

A Case for Diagnosis (Keratosis Palmaris et Plantaris, Acquired Type, or Haxthausen's Disease?). Presented by DR. HOWARD EARLE TWINING

A. R., a white woman aged 44, about a year ago began to notice a progressive thickening of the palms and soles. She does not complain of itching or burning but does have pain due to cracks and fissures. There is no hyperhidrosis. The hands show a decided thickening of the epidermis, which not only involves the palms but extends onto the extensor surfaces of the fingers and the backs of the hands as well. The nails are only slightly involved. The extensor surfaces of both forearms to the elbows are also somewhat thickened and scaly. The soles are symmetrically hyperkeratotic, in some areas about 0.75 cm. in diameter, especially over pressure areas. The ankles are comparatively free. An erythematous contiguous border extends over the heel and lateral aspects of the feet. Some of the toe nails are thickened. The interdigital webs are comparatively free. The Wassermann and Kahn reactions of the blood were negative. There were no fungi in scrapings. The patient has been given estrone, 1 cc. intramuscularly twice weekly, and 10 per cent salicylic acid ointment, with decided improvement after three weeks.

DISCUSSION

DR. FRED D. WEIDMAN: This woman has had rheumatism for several years. The combination of these keratotic lesions makes one think of gonococcic infection. Has this possibility been investigated? I do not recall having seen gonorrheal keratosis in a female.

DR. HOWARD EARLE TWINING: This patient was studied in the gynecologic and orthopedic departments before she was referred to me, but so far as I know there was no test made for gonorrhea. The history of keratosis coming on about

three years ago after complete hysterectomy suggested that the patient may have keratoderma climactericum, and for that reason she was treated with estrone for three weeks. Under this therapy the lesions have cleared up anywhere from 25 to 30 per cent.

A Case for Diagnosis (Fibrositis Circumscripta? Paraffinoma?). Presented by DR. MARJORY HARDY (by invitation), Norristown, Pa.

L. W., a Negress aged 52, was first seen on Jan. 5, 1940. On the outer aspect of the upper part of the left arm the patient had an infiltrated plaque, 12.7 cm. long and 6.3 cm. wide. The skin over the lesion was intact. She stated that the area had been present two years. There was no history of injury to the arm and no history of infections at the site. The area is somewhat smaller and definitely less infiltrated since the patient has received 0.32 Gm. of ammonium chloride three times a day. The Wassermann reaction of the blood was negative.

DISCUSSION

DR. FRED D. WEIDMAN: I was impressed by the warmth of the lesion. This suggests a continued inflammatory process, which would hardly fit in with scleredema adultorum. The condition would have to be a remarkably localized example of that disease, and I could not get any history of a febrile state at the onset. I doubt that trichinosis would be the cause. A biopsy should be performed.

DR. MORRIS MARKOWITZ: I suggest fibrositis circumscripta. The skin covering the lesion seems to be free.

DR. BERTRAM SHAFFER (by invitation): In Weber's original article on relapsing nonsuppurative nodular panniculitis (Weber, F. P.: A Case of Relapsing Nonsuppurative Panniculitis Showing Phagocytosis of Subcutaneous Fat Cells by Macrophages, *Brit. J. Dermat.* **27**:301, 1925), he mentioned cases of localized fibrositis of this type. I think this condition would easily fall into this category.

DR. JOSEPH V. KLAUDER: The lesion appears to me to be attached to the skin and not to involve the muscle.

DR. VAUGHN C. GARNER: I think one must consider the possibility of paraffinoma, though I know the patient states that she has never received injections of paraffin.

Correspondence

SUPERFICIAL NONINFLAMMATORY LESIONS OF THE FEET

To the Editor:—I should like to make the following observations relative to the article by Dr. Sutherland-Campbell, on "Superficial Noninflammatory Lesions of the Feet" (ARCH. DERMAT. & SYPH. **41**:6 [June] 1940). The conditions described have been repeatedly observed by most dermatologists but have not been reported. The same situation existed some years ago relative to Shamberg's disease. The interesting point in this report is the finding of a fungous structure.

I have personally observed and prescribed for a number of these conditions and have invariably found them associated with warts. The wart, however, has not been the usual plantar type but has consisted of closely grouped lesions, the centers of which have been filled with a crumbly material which can be pricked out entirely with a knife. When this has been done the floor of the lesion is flat and does not have the bleeding points of the usual verruca vulgaris. These lesions have shown an unusual resistance to heavy roentgen therapy, and if they have disappeared they reappear surprisingly in the same location. They also resist other forms of destructive treatment to a considerable degree. I have called these lesions "aggregate warts." If these lesions occur on the sole, in the presence of considerable moisture, particularly in contact with composition and nonabsorptive inner soles, they assume the characteristics of the condition described by Dr. Sutherland-Campbell. When this form has been assumed it approaches the state of porokeratosis. I consider that this form is simply a modification of the wartlike type due to pressure and maceration.

I have found that these conditions respond to compound ointment of benzoic acid N. F., but they will also respond to a considerable degree to dry footwear.

It is interesting that Dr. Sutherland-Campbell has demonstrated a fungus within the lesion, and if this can be proved to be the causative organism the present conception of this particular form of wart will probably have to be modified.

MERLIN T.-R. MAYNARD, M.D., San Jose, Calif.

Directory of Dermatologic Societies *

INTERNATIONAL

Tenth International Congress of Dermatology and Syphilology

Oliver S. Ormsby, President, 25 E. Washington St., Chicago.
Paul A. O'Leary, Secretary-General, 102–2d Ave. S. W., Rochester, Minn.
Place: New York. Time: Postponed indefinitely.

Pan American Medical Association, Section of Dermatology and Syphilology

Elmore B. Tauber, President, 19 W. 7th St., Cincinnati.
Austin W. Cheever, Secretary, 49 Bay State Rd., Boston.

FOREIGN

British Association of Dermatology and Syphilology (Canadian Branch)

L. P. Ereaux, President, 1390 Sherbrooke St. W., Montreal.
F. E. Cormia, Secretary-Treasurer, 2068 Sherbrooke St. W., Montreal.

Royal Society of Medicine, Section of Dermatology

H. W. Barber, President, 7 Devonshire Pl., London, W. 1, England.
Louis Forman, Secretary, 7 Devonshire Pl., London, W. 1, England.

NATIONAL

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

J. Gardner Hopkins, Chairman, 102 E. 78th St., New York.
C. F. Lehmann, Secretary, 705 E. Houston St., San Antonio, Texas.
Place: Cleveland.

American Academy of Dermatology and Syphilology

Harry R. Foerster, President, 208 E. Wisconsin Ave., Milwaukee.
Earl D. Osborne, Secretary, 471 Delaware Ave., Buffalo, N. Y.
Place: Philadelphia.

American Board of Dermatology and Syphilology

Howard Fox, President, 140 E. 54th St., New York.
C. Guy Lane, Secretary-Treasurer, 416 Marlborough St., Boston.

American Dermatological Association

Frank C. Knowles, President, 2035 Spruce St., Philadelphia.
Fred D. Weidman, Secretary, University of Pennsylvania, Philadelphia.

Society for Investigative Dermatology

John H. Stokes, President, 4228 Spruce St., Philadelphia.
S. W. Becker, Secretary, University of Chicago, Department of Medicine, Chicago.

* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

SECTIONAL

Central States Dermatological Association

John C. Kerr, President, 621–14th St., Wheeling, W. Va.
Marvin B. Goldstein, Secretary-Treasurer, Stambaugh Bldg., Youngstown, Ohio.

Mississippi Valley Dermatological Society

Daniel J. Kindel, President, 1910 Union Central Bldg., Cincinnati.
Lawrence Goldberg, Secretary-Treasurer, Doctors Bldg., Cincinnati.
Place: Chicago.

New England Dermatological Society

J. Harper Blaisdell, President, 83 Marlborough St., Boston.
Bernard Appel, Secretary, 483 Beacon St., Boston.

Northern New Jersey Dermatological Society

N. B. Heller, President, 31 Lincoln Pk., Newark.
C. C. Carpenter, Secretary, 38 Waldron Ave., Summit.
Place: Academy of Medicine of Northern New Jersey, Newark. Time: Third Tuesday of March, April, October and December.

Southeastern Dermatological Association

J. R. Allison, Chairman, 1121 Barnwell St., Columbia, S. C.
Howard King, Secretary, 328 Doctors Bldg., Nashville, Tenn.

Southern Medical Association, Section on Dermatology and Syphilology

Howard Hailey, Chairman, 107 Doctors Bldg., Atlanta, Ga.
John H. Lamb, Secretary, 117 N. Broadway, Oklahoma City.

STATE

California Medical Association, Scientific Assembly, Dermatology and Syphilology Section

Nelson Paul Anderson, Chairman, 2007 Wilshire Blvd., Los Angeles.
Julius R. Scholtz, Secretary, 1930 Wilshire Blvd., Los Angeles.

Connecticut State Medical Society, Section on Dermatology

Michael J. Morrisey, Chairman, 18 Asylum St., Hartford.
Harry Bailey, Secretary, 242 Trumbull St., Hartford.

Florida Society of Dermatology and Syphilology

Alan D. Brown, Chairman, 117 W. Duval St., Jacksonville.
Lauren M. Sompayrac, Secretary, 459 St. James Bldg., Jacksonville.

Louisiana Dermatological Society

M. T. Van Studdiford, President, 912 Pere Marquette Bldg., New Orleans.
R. A. Oriol, Secretary-Treasurer, 921 Canal St., New Orleans.

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C. Guy Lane, President, 416 Marlborough St., Boston.
J. G. Downing, Secretary, 520 Commonwealth Ave., Boston.

Medical Society of the State of New York, Section on Dermatology and Syphilology

Frank C. Combes, Chairman, 80 W. 40th St., New York.
Rudolph Ruedemann Jr., Secretary, 256 State St., Albany.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA, SECTION ON DERMATOLOGY

Vaughn C. Garner, Chairman, Germantown Professional Bldg., Philadelphia.
Bernhard A. Goldmann, Secretary, 500 Penn Ave., Pittsburgh.

MICHIGAN STATE MEDICAL SOCIETY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Frank Menaugh, Chairman, Ford Hospital, Detroit.
Eugene A. Hand, Secretary, 801 Second National Bank Bldg., Saginaw.

MINNESOTA DERMATOLOGICAL SOCIETY

Carl W. Laymon, President, 345 Medical Arts Bldg., Minneapolis.
F. W. Lynch, Secretary-Treasurer, 317 Lowry Medical Arts Bldg., St. Paul.
Time: First Friday in October, December, February and April.

OKLAHOMA STATE DERMATOLOGICAL SOCIETY

John H. Lamb Jr., President, 117 N. Broadway, Oklahoma City.
Onis G. Hazel, Secretary, 1200 N. Walker, Oklahoma City.

TEXAS DERMATOLOGICAL SOCIETY

Leslie Smith, President, 109 N. Oregon St., El Paso.
Duncan O. Poth, Secretary, 414 Navarro St., San Antonio.

LOCAL

BALTIMORE-WASHINGTON DERMATOLOGICAL SOCIETY

Walter Teichmann, President, 1726 I St. N. W., Washington, D. C.
Russell J. Fields, Secretary, 1726 I St. N. W., Washington, D. C.
Place: Alternate cities. Time: Third Thursday of each month.

BRONX DERMATOLOGICAL SOCIETY

Marion B. Sulzberger, President, 962 Park Ave., New York.
Henry Silver, Secretary, 290 West End Ave., New York.

BROOKLYN DERMATOLOGICAL SOCIETY

M. J. Cantor, President, 907 St. Marks Ave., Brooklyn.
S. H. Silvers, Secretary, 920 Bushwick Ave., Brooklyn.
Time: Third Monday of each month except June, July, August and September.

BUFFALO-ROCHESTER DERMATOLOGICAL SOCIETY

Richard L. Saunders, President, 333 Linwood Ave., Buffalo.
James W. Jordan, Secretary, 471 Delaware Ave., Buffalo.

CENTRAL NEW YORK DERMATOLOGICAL SOCIETY

Leon H. Griggs, President, 1804 State Tower Bldg., Syracuse.
Maxwell C. Snider, Secretary, 106 Oak St., Binghamton.

CHICAGO DERMATOLOGICAL SOCIETY

Herbert Rattner, President, 25 E. Washington St., Chicago.
Michael H. Ebert, Secretary-Treasurer, 25 E. Washington St., Chicago.

CINCINNATI SOCIETY OF DERMATOLOGY AND SYPHILOLOGY

Elmore B. Tauber, President, 19 W. 7th St., Cincinnati.
Lawrence C. Goldberg, Secretary-Treasurer, 623 Doctors Bldg., Cincinnati.
Place: Cincinnati. Time: First Wednesday of each month, except July, August and September.

Cleveland Dermatological Society

C. L. Baskin, President, 159 S. Main St., Akron, Ohio.
Charles G. La Rocco, Secretary, 2060 E. 9th St., Cleveland.

Detroit Dermatological Society

A. R. Woodburne, President, 612 Medical Arts Bldg., Grand Rapids, Mich.
Ruth Herrick, Secretary-Treasurer, 528 Medical Arts Bldg., Grand Rapids, Mich.

Kansas City (Mo.) Dermatological Society

C. C. Dennie, President, 1103 Grand Ave., Kansas City.
Thomas B. Hall, Secretary, 902 Professional Bldg., Kansas City.

Los Angeles Dermatological Society

Chris R. Halloran, President, 1052 W. 6th St., Los Angeles.
Saul S. Robinson, Secretary, 1930 Wilshire Blvd., Los Angeles.
Time: Second Tuesday of each month, October to May, inclusive.

Manhattan Dermatologic Society

J. Frank Fraser, Chairman, 115 E. 61st St., New York.
Anthony C. Cipollaro, Secretary, 40 E. 61st St., New York.

Montreal Dermatological Society

L. P. Ereaux, President, 1390 Sherbrooke St. W., Montreal, Canada.
Paul Poirier, Secretary, 456 Sherbrooke St. E., Montreal, Canada.

New York Academy of Medicine, Section of Dermatology and Syphilis

E. William Abramowitz, Chairman, 853–7th Ave., New York.
Lewis B. Robinson, Secretary, 102 E. 78th St., New York.

New York Dermatological Society

Frank C. Combes, President, 80 W. 40th St., New York.
J. Gardner Hopkins, Secretary-Treasurer, 102 E. 78th St., New York.

Omaha Dermatological Society

Donald J. Wilson, President, 1113 Medical Arts Bldg., Omaha.
Leonard J. Owen, Secretary-Treasurer, 954 Stuart Bldg., Lincoln, Neb.

Philadelphia Dermatological Society

Herman Beerman, Chairman, 255 S. 17th St., Philadelphia.
Donald M. Pillsbury, Secretary, 133 S. 36th St., Philadelphia.
Time: Third Friday of each month from September to May, inclusive.

Pittsburgh Dermatological Society

Marvin B. Goldstein, President, Stambaugh Bldg., Youngstown, Ohio.
Charles L. Schmitt, Secretary, Medical Arts Bldg., Pittsburgh.
Time: Third Thursday of every month except July and August.

St. Louis Dermatological Society

Martin F. Engman Jr., President, 3720 Washington Blvd., St. Louis.
Joseph Grindon Jr., Secretary-Treasurer, 323 Lister Bldg., St. Louis.
Place: Barnard Free Skin and Cancer Hospital. Time: 2 p. m., second Wednesday of each month.

San Francisco Dermatological Society

Frances A. Torrey, President, 123 Pemberton Pl., San Francisco.
H. V. Allington, Secretary, 3115 Webster St., Oakland, Calif.
Time: Third Friday of February, April, September and November.